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CANNON REVISITED; EMOTIONS AND BODILY CHANGES: THEIR RELEVANCE TO DISEASE.[1]

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IT is 30 years since the publication of W. B. Cannon's (1929) classical work "Bodily Changes in Pain, Fear, Hunger and Rage". In this book, Cannon clearly pointed out the possible relevance of these observations in animals to disease states in man. It is of interest to inquire to what extent our more extensive knowledge today has confirmed or denied Cannon's formulations.

During his student days, Cannon showed some interest in the field of neurology and psychiatry. His work on emotions and bodily changes was initiated through a chance observation during his early studies on gastric function in animals in the Physiology Department at Harvard Medical School; he noted what happened to a cat's stomach when it saw a dog. Cannon went on to demonstrate the familiar pattern of tachycardia, pupillary dilatation, erection of hair, sweating, decreased clotting time, increased red blood cell count, increase in blood sugar level and splanchnic vasoconstriction and inhibition of digestion, which occurs during states of considerable emotional disturbance. Using an intestinal muscle preparation and a denervated cat's heart, he was able to show that there was an increase in the amount of adrenaline in the circulating blood in association with these changes. He was subsequently able to demonstrate that adrenaline reproduced most of these changes, while they did not occur in the absence of the adrenal gland. He was led to postulate the importance of adrenaline and the sympathetic nervous system in bodily responses to environmental stimuli. He suggested that such transient physiological changes could be prolonged, with the production of symptoms and diseases in human subjects. The concept of the conditioned reflex proposed by Pavlov shortly before this indicated to Cannon the possibility that these changes could be prolonged as a result of conditioning factors.

Selye, in the light of the demonstration of potent adrenal cortical extracts in the early thirties by Swingle and Harrop, was led to postulate the importance of the adrenal cortex in relation to environmental stimuli. He recognized that a variety of stimuli such as exposure to cold, infection, intoxication and fatigue produced a common pattern of bodily response in rats, characterized by enlargement of the adrenal cortices, involution of the thymico-lymphatic tissue and the appearance of gastric ulcers (Selye, 1936). This pattern of changes, called the "alarm reaction" by Selye, could be abolished by previous hypophysectomy, thus indicating that the pituitary and adrenal cortex were participating in this response. He

[1] A post-graduate lecture delivered for the Australian Association of Psychiatrists (Victorian Branch), under the auspices of the Melbourne Medical Post-Graduate Committee, at the Royal Melbourne Hospital on April 9, 1959.

also recognized that emotional disturbance could produce a similar pattern.

Selye subsequently showed that chronic exposure of animals to such stimuli produced pathological changes in various organs, such as the kidneys and heart. These changes could be reproduced by the administration of certain hormones, such as desoxycorticosterone and pituitary extracts. An important adjuvant factor in these changes with both cold and hormones was a high salt intake. On the basis of this evidence, Selye has suggested that certain diseases in man, such as those of the collagen group, are due to adrenal dysfunction with over-production of mineralo-corticoids. The merits of this hypothesis are still uncertain. The discovery of the natural mineralo-corticoid aldosterone in 1953 has paved the way for methods of assay of this hormone in these disease states, but definitive data are not yet available. So far, Selye's major contribution has been to recognize the common pattern of response to a variety of stimuli involving the adrenal cortex, as Cannon recognized the adrenal medulla.

Human Studies.

Wolff and Wolf with their co-workers at New York Hospital have documented for man the pattern of physiological changes described by Cannon in animals (Wolff, 1952). Beginning with the classical studies on Tom's gastric fistula in 1944, they passed on to further mucous membranes, such as the colon (using the opportunity of colostomy) and the nose. Then the reactions of the skin and the circulatory system were studied, and finally the endocrine glands and metabolism; in this last phase I was privileged to take part. Cannon's concepts derived from animal studies have been somewhat revised as a result of this work in man. Wolff, following Cannon, has emphasized the biological value of many of these responses, calling them protective reaction patterns, but he points out that in man fragmentation tends to occur, so that patterns involving single organs can be defined—"the principle of parsimony" (Wolff, 1952). This work has also shown that there is some association between specific psychological attitudes and different bodily changes. There appeared to be a certain biological meaning in this attitude, in that it often described the physiological process itself, for example, patients developing urticaria in association with emotionally provoking stimuli often felt as though they were "beaten up". Studies revealed that they made remarks such as "I was taking a beating"; "the boss cracked the whip on me"; "my mother was hammering on me". The urticarial response itself closely resembles the triple response of Lewis, a response which has been shown to follow physical injury to the skin. These patients seem to be reacting as though they had experienced a physical injury, even though no blow had been delivered.

Other attitudes in association with other bodily responses have been described in detail by Grace and Graham (1953). It is of interest that patients with cold hands and those with emotionally provoked Raynaud's phenomenon use expressions such as "I wanted to hit him", "I wanted to put a knife through him", or "I wanted to strangle him". In a recent study, Graham *et alii* (1958) were able to induce these attitudes in patients under hypnosis, and they were able to show that the skin temperature was significantly higher in association with the attitude characteristic of patients with urticaria than it was in association with attitudes characteristic of Raynaud's phenomenon. These findings indicate that the occurrence of a particular reaction pattern can be predicted to some extent by the attitude of the patient.

The reasons for the differences in attitude in relation to essentially the same stimuli are not fully understood, but there is evidence that both genetic and environmental factors are important. The predominant relationship in childhood, for example, is important, as is the pattern of child care (restrictive or permissive) and the occurrence of deprivation. It seems most profitable to regard the attitude and the bodily reaction pattern as two facets of a response of the whole organism, rather than as being causally related. This is a position of psychophysical parallelism. Grace and Graham have suggested that the word "emotion" be defined as a particular attitude (meaning how the patient sees himself in a given situation, and what he wants to do about it), together with the associated bodily changes.

Neurophysiology is now providing a basis for the understanding of the mechanisms involved in this psycho-physical response. Gerard (1958) has pointed out that there are four gradations of response to stimuli: (i) the automatic response; (ii) the unconscious response; (iii) the conscious response; (iv) emotion. If a stimulus is not removed by an automatic response, sensory impulses accumulate, producing summation, radiation and eventually reverberation in the central nervous system. A certain degree of activation of the hypothalamus, the reticular formation and the limbic system is associated with emotion and a pattern of neuro-endocrine discharge involving the autonomic nervous system, the pituitary, the adrenal glands and the thyroid gland. At first performance is improved, but, as the excitation of neurones increases, performance tends to become more rigid, then deterioration occurs and finally the patient develops the syndromes of neurosis and psychosis. Psychosomatic disorders are also regarded as by-products of this increase in neurone excitation. In many of these subjects performance remains good, even though organ dysfunction has occurred. Many of these patients are, in fact, bearing burdens of great responsibility and exacting work. In others, the disturbance follows bereavement or loss of an important source of emotional support.

As has already been indicated, we may distinguish various fragmented patterns in this neuro-endocrine discharge, called by Cannon the "downward discharge".

First, patterns involving autonomic activation, such as gastric hyperfunction and hypofunction, similar patterns in the colon and changes in the blood vessels of the skin have already been described. These studies are well known, and will not be reviewed in detail here. Studies on Tom reveal a similar pattern of response in the gastric mucosa with food, stressful interviews and spontaneous stressful occurrences (Wolff, 1952). Prolongation of this pattern can produce so-called structural or organic disease; for example, in the state of hyperfunction of the stomach, the congested mucosa readily develops ulceration and bleeds. Such observations appear to provide the basis for understanding the occurrence of acute ulceration of the stomach and gastric hæmorrhage in man under conditions of life stress.

More recent work has been concerned with the occurrence of changes in endocrine secretion, and we shall consider in turn the adrenal medulla, the adrenal cortex and the thyroid gland.

Adrenal Medulla.

As Cannon anticipated, it is now known that the adrenal medulla produces two secretions—adrenaline and noradrenaline. Although their effects are equal on the rat colon the hormones can be differentiated by their effect on the rat uterus. Noradrenaline is concerned with the maintenance of blood pressure. It is also continually secreted at autonomic nerve endings, so that its level in the body is not significantly affected by adrenalectomy. Adrenaline is produced sporadically in relation to environmental stimuli, as Cannon demonstrated. There is a considerable diurnal variation in output of these two hormones, especially that of adrenaline, which is greatly increased during the day.

The results of urine assays carried out under a variety of conditions of emotional provocation have been reported by Elmadjean, from the Worcester Institute, U.S.A. (1958). Lysergic acid diethylamide in a dosage of 150 to 300 microgrammes has been shown to cause a marked

rise in adrenaline secretion in a small group of four manic depressives, and in three involutional melancholic patients with marked emotional disturbance. On the other hand, in seven schizophrenics there was neither an adrenaline response nor an emotional response. In anticipatory states in normal subjects, under the conditions of laboratory study, normal rates of excretion were shown under conditions of relaxation and tranquillity. On the other hand, in subjects who were restless, constantly questioning and in an obvious state of apprehension, increases both in adrenaline and in noradrenaline were shown.

Under conditions of competitive sport, for example in players just before an ice hockey game, noradrenaline secretion increased six times. In players sitting on the sidelines there was only a slight increase in noradrenaline, but a marked increase in adrenaline secretion. In one player involved in a fist fight, noradrenaline secretion was markedly increased. Studies on amateur boxers before a fight revealed considerable variation: for example, one who shadow-boxed for five minutes before he went into the ring showed a high noradrenaline secretion; in another who sat quietly waiting his turn, no rise in noradrenaline secretion occurred. If there was a sense of great anticipation, adrenaline excess could be demonstrated, as also with a very close fight.

In psychotic patients, a relation between noradrenaline and aggressive behaviour could be shown. Studies during psychotherapy in both therapist and patient revealed considerable changs in both. Elmadjean suggests that these findings are consistent with previous indirect data suggesting that a state of active aggression and anger is associated with increase in noradrenaline secretion (of the order of 0·2 μg. per kilogram per minute). On the other hand, a passive state of fear with self-effacement is associated with adrenaline increase (0·1 μg. per kilogram per minute).

It is of interest that these findings have some support from observations in animals. For example, a rabbit and guinea-pig have a predominant adrenaline secretion, while the lion has been shown by Goodall, as a result of a special expedition to Africa (during which he shot a lion himself) to produce noradrenaline.

The results of these studies on the adrenal medullary secretions confirm observations made on circulatory patterns by means of a ballistocardiograph. It is now well known that no absolute deductions can be made about cardiac output or peripheral resistance by this technique, but patterns of change characteristic of adrenaline and noradrenaline have been described.

In a study of 69 healthy students doing abstruse mathematical problems, Funkestein *et alii* (1954) have shown that there was a correlation between the adrenaline pattern and those who became angry with themselves (30%). On the other hand, there was a correlation between the noradrenaline pattern and those who became angry with the examiner (also 30%). It has been suggested that the choice of these patterns may depend on childhood experiences; for example, those who became angry with themselves have a dominant mother, while those whose anger is directed outwards have a dominant father.

In studies on hypertensive patients, Wolf *et alii* (1955) have shown that both patterns occur. No significant differences could be shown between patients with normal or elevated blood pressure, while sympathectomy did not alter these responses. Moses *et alii* (1956) have confirmed the existence of a high peripheral resistance pattern with rage and resentment in hypertensive patients. Less marked, but similar, changes were seen with inhibited emotional expression, while expression of feeling was associated with an increased cardiac output pattern.

Adrenaline was shown by Cannon to cause a sharp decrease in clotting time, at the same time as a pressor response. Schneider (1950) has been able to show increase in blood viscosity, with shortening of the clotting time and elevation of the blood sedimentation rate, in association with interviews arousing personal conflicts with resentment. Elevation of blood pressure was also noted under these conditions. Similar observations have been made during spontaneous stressful situations in a group of accountants at the time of lodging income tax returns (Friedman *et alii*, 1958).

We may conclude, therefore, that there is good evidence that the disturbances described by Cannon in animals occur in man. There is evidence that these patterns vary with different emotional states. In particular, there is a difference between the self-assertive state of anger and the submissive state of fear—a difference not apparent to Cannon in his earlier studies on animals.

Adrenal Cortex.

With the availability of methods of measuring the adrenal cortical hormones in blood and urine, evidence is now available on changes in these secretions in association with emotional disturbance. The main secretions are hydrocortisone and aldosterone. These hormones have been measured both free in the blood and in the form of metabolites in the urine.

Observations under the conditions of everyday situations have revealed considerable increase in urine 17-hydroxycortisteroid excretion (Hetzel *et alii*, 1955) and also increase in aldosterone secretion (Venning *et alii*, 1958). Similar changes could be shown with stressful interviews (Hetzel *et alii*, 1955; Bliss *et alii*, 1956). Under conditions of competitive sport, Hill et alii (1956) have shown changes in urine steroid excretion in both cox and crew in the Harvard-Yale boat race. It is apparent that such changes are primarily related to the emotional rather than to the exercise component.

Gemzell *et alii* (1955) have shown, in patients awaiting operation, elevation in blood corticoid levels as high, in several cases, as those after surgery. There was a mean increase from 5·5 to 14·5 μg. per 100 ml. on the day before the operation. Price *et alii* (1957) have been able to correlate these increases in blood corticoid levels in patients before operation with the appearance of emotional disturbance, as indicated by independent testing rather than by psycho-pathological features such as morbid preoccupation. They suggest that this elevation may be associated with a number of different emotional states, with the relatively undifferentiated component of "stress involvement".

Observations on patients with acute psychiatric disorders on their admission to hospital have been reported by Board *et alii* (1956). A significant rise in blood 17-hydroxycorticosteroid level has been observed, particularly in patients with retarded depressive states. This level tended to subside as retardation decreased. Those patients given shock therapy showed a significantly higher level than those who did not require shock therapy. These authors suggest that the degree of elevation is directly related to inability to express emotion.

The Thyroid.

There is evidence of elevation of circulating thyroid hormone in similar conditions to those already described for adrenal cortical hormones (Hetzel *et alii*, 1956; Board *et alii*, 1956). However, the changes are, on the whole, less marked. Board *et alii* (1956) found the elevated level in depressive patients subsided earlier than that of the blood corticoids, and suggested that there were three sequential reactions under these conditions—first, adrenaline increase, then increase in adrenal cortical hormones, and finally increase in thyroid hormones. However, under other conditions, such as cold, thyroid activation occurs prior to adrenal activation (Brown-Grant *et alii*, 1956).

Metabolic Responses.

Such profound disturbances in endocrine secretion would be expected to be associated with metabolic changes. Hetzel *et alii* (1956) have shown an increase in metabolic rate with a fall in respiratory quotient, and an increase in nitrogen and electrolyte excretion

during stressful interviews, sometimes in association with elevation of serum protein-bound iodine level and urinary 17-hyroxycorticosteroid excretion. The occurrence of these changes has been associated with feelings of dread and horror. Interviews eliciting resentment predominantly were not associated with such changes. It has been suggested that their mechanism involves adrenaline, and adrenal cortical and thyroid activation. As Cannon anticipated, it has been shown that thyroid hormones augment the metabolic response to adrenaline, and the same is true of some of the effects of hydrocortisone (Hetzel *et alii*, 1957, 1958, 1959).

The significance of these findings is that another stimulus productive of catabolism has been defined, so that factors such as emotional disturbance as well as infection must be taken into account in the management of patients with renal disease, diabetes mellitus (Hinkle and Wolf, 1952) or other metabolic disorders.

A variety of disturbances in fluid and electrolyte metabolism have been described by Schottstaedt *et alii* (1956) in association with various emotional states. Patterns of diuresis and retention of sodium, potassium and water have been demonstrated, which may be clinically significant, for example in the precipitation of congestive failure.

Relation to Disease.

The question arises as to the significance of these transient physiological changes for disease states in man. Suggestive evidence is available from various sources.

Epidemiological Evidence.

There is a relationship between the incidence of stress and the occurrence of certain diseases, for example, hyperthyroidism occurred in epidemic form in Europe after the German occupation (Wolff, 1952). Coronary disease tends to affect men with a heavy load of responsibility—for example general practitioners and surgeons—as opposed to those in more sheltered medical specialties (Morris *et alii*, 1952). The high incidence of New Australians among patients suffering from common ante-natal complications of pregnancy—for example, prolonged labour and prolonged vomiting (Hetzel *et alii*, 1959)—suggests a relation between these complications and problems of adjustment in a new country. These associations require to be followed up with intensive studies of patients suffering from particular disease states.

Evidence from Case Studies.

Case studies have demonstrated the relation between stress and various disease states. Cannon suggested, in the light of Pavlov's work, that disease could result from prolonged psycho-physiological disturbance. There is much evidence of the importance of emotional provocation in the precipitation of disease conditions such as peptic ulcer, ulcerative colitis, bronchial asthma and hyperthyroidism. In a study (Hetzel, 1954) of 40 unselected patients with hyperthyroidism at New York Hospital, a precipitating episode could be demonstrated in all cases but one within three months of the onset of symptoms. These consisted of the following: (i) loss of a loved one by death, desertion or separation (18 cases); (ii) threat of loss of a loved one (10 cases); (iii) loss of financial and social security through business failure or forced migration (11 cases). The attitude of these patients in this situation indicated a keen sense of loss akin to that of being stranded. For example in group (i), one patient said "I felt like the bottom had dropped out of everything"; in group (ii), another—a German migrant aged 30 years whose mail had been delayed—said "I am like a little boy crying after he had lost his mother"; in group (iii) yet another said "My wife felt I was a failure". These patients develop an aggressive self-sufficiency which often leads to their refusing to consult doctors, unless forced by friends who notice the obvious signs of exophthalmos. Similar factors can be shown in a number of other psychosomatic disorders, although the attitudes expressed by the patients differ (Wolff, 1952). Psychoanalytical investigations have assisted understanding of the psychodynamics involved in these reaction patterns (Ham *et alii*, 1950).

A controlled study of 50 primiparæ suffering from pre-eclamptic toxæmia has recently been reported (Coppen, 1958). A comparison was made between these patients and 50 patients with normal pregnancies. This study revealed an increased incidence of premenstrual tension, poor sexual adjustment, emotionally disturbed menarche, disturbed attitude to pregnancy and a high neuroticism score on the Maudsley personality inventory. Measurement of the patients' physique showed a tendency to abnormal androgyny with increased transverse chest diameter. There was an increased incidence of stressful experience associated with family life during pregnancy. It was concluded that there was evidence of poor adjustment to the familial role in these patients with toxæmia. We have been carrying out a similar study in Adelaide, and have been able to confirm some of these findings. Similar controlled studies of patients with prolonged labour and prolonged vomiting in pregnancy have also been published (Cramond, 1954; Coppen, 1959). The ready availability of control groups in these pregnancy studies makes them particularly valuable. They provide strong evidence of the importance of stress in these conditons, though it is apparent that it is unprofitable to think in terms of stress as a single cause.

Predictive Evidence.

If there is a relation between a stressful situation and the onset of a disease state, it should be possible to predict the occurrence of a disease state from this knowledge, and thus go some distance towards satisfying Koch's postulates. A study of the occurrence of duodenal ulcer in a group of 2073 army inductees goes some way to meeting these requirements (Wiener *et alii*, 1957). Serum levels of pepsinogen were determined in this group. Two groups of 63 (comprising the upper 15% of the original group) and 57 (the lower 5%) were subjected to psychological testing and barium meal examination. One of the subjects in the first group was demonstrated to have a duodenal ulcer. Four months later these subjects were again submitted to barium meal X-ray examination and nine of the upper 15% (eight of whom were in the upper 5% of the original group) were shown to have a duodenal ulcer, indicating a strong association between high serum pepsinogen level and duodenal ulceration. Classification of the subjects on the results of the psychological tests indicated an 85% correlation between those results and the two groups showing high and low pepsinogen levels in both groups. This classification was made according to the known characteristics of ulcer patients—namely, major unresolved conflicts about dependency and oral gratification.

It was concluded that neither high gastric secretion nor a specific psychodynamic constellation was enough to produce an ulcer. Together, however, with the stimulus of a stress-producing social situation these two factors constituted the essential determinants producing peptic ulcer.

We have, therefore, to consider the following three factors in accounting for a disease state:

1. A genetic factor, evident for example in hypertension, diabetes and migraine with their strong familial tendencies. The importance of genetic factors in other conditions such as peptic ulcer (revealed by blood group distribution and determinations of serum pepsinogen level at birth) and rheumatoid arthritis (serum factor) has been recently demonstrated.

2. A specific psychodynamic background arising primarily from childhood experiences.

3. A current stressful life situation.

The suggestion is that a specific disease state will not occur in the absence of any one of these factors.

An interesting and successful attempt was made to recognize pre-hypertensive subjects among a group of 40 college students in San Francisco (Harris *et alii*,

1953). These students were interviewed by a psychiatrist who had previously studied 100 hypertensive patients, and had come to certain conclusions about their personality characteristics. On the basis of these conclusions, he was able to identify correctly 26 of 38 subjects ($P < 0.02$). Exposure of the students to two experimental psychodramas was carried out to see whether any difference in behaviour could be correlated with elevation of blood pressure. Adjectives describing behaviour were checked by the observers. Pre-hypertensive students (those with blood pressures greater than 140/90 mm. of mercury) were described as more involved, less well controlled and organized, creating an unfavourable impression, while those with normal blood pressure were described as more adaptable, independent, mature and collected. It is of interest that the students themselves used similar expressions to describe their behaviour, such as, in the case of pre-hypertensive subjects, "eccentric", "hot-headed", "moody", "rash", "tense" and "hurried". It was concluded that pre-hypertensive subjects were more prone to emotional disturbance with concomitant rise in blood pressure.

Results of Treatment.

If there is a significant relation between a stressful life situation and the occurrence of a disease state, it should be possible, by relieving the stressful situation, to halt the course of the disease. There is evidence available that this can be done.

Matched series of patients with peptic ulcer and ulcerative colitis have been studied at the New York Hospital (Grace *et alii*, 1954). A comparison has been made between a series of patients treated in a clinic where specific attention was paid to the environmental factor, and the results have been compared with those obtained in patients treated with diet, drugs and sound medical management, but no specific attention to the environmental factor.

Statistical analysis showed a significantly better result, as indicated by a lowered mortality, lowered incidence of complications and lowered rate of surgical intervention, in the group receiving special attention to the stress factor in their illness. These results were obtained by physicians spending more time with their patients, especially in the early stages of their illness, than is customary in busy medical out-patient clinics. They do indicate that it is possible to alter the course of such conditions by specific attention to the stress factor.

Conclusion.

Pragmatic considerations continue to dominate our management of these disorders. These usually, though not always, lead to therapy directed to the end organ—by the use of drugs or by surgical means. However, for the individual patient, the emotional factors must be kept in mind continually if clinical medicine is not to become a mechanical practice. With the increasing control of infections, emotionally provoking stimuli have become numerically more important. For this reason, Cannon's original contribution, and the subsequent studies inspired by him, are of considerable importance in the study and management of human disease.

As Cannon himself remarked:

> Escape from the insistent demands of the pathologists for structural evidence of disease and also from the vagueness and mysticism of the psychological healers can be found in an understanding of the physiological processes which accompany deep emotional disturbances.

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References.

BLISS, E. L., MIGEON, C. J., BRANCH, C. H. H., and SAMUELS, L. T. (1956), "Reaction of the Adrenal Cortices to Emotional Stress", *Psychosom. Med.*, 18: 56.

BOARD, F., PERSKY, H., and HAMBURG, D. A. (1956), "Psychological Stress and Endocrine Functions", *Psychosom. Med.*, 18: 324.

BROWN-GRANT, K. (1956), "Changes in Thyroid Activity of Rats Exposed to Cold", *J. Physiol. (Lond.)*, 131: 52.

CANNON, W. B. (1929), "Bodily Changes in Pain, Hunger, Fear and Rage", second edition, Appleton, New York.

COPPEN, A. J. (1959), "Vomiting of Early Pregnancy — Psychological Factors and Body Build", *Lancet*, 1: 172.

COPPEN, A. J. (1958), "Psychosomatic Aspects of Pre-Eclamptic Toxæmia", *J. psychosom. Res.*, 2: 24.

CRAMOND, W. A. (1954), "Psychological Aspects of Uterine Dysfunction", *Lancet*, 2: 1241.

ELMADJEAN, F., HOPE, J. M., and LAWSON, E. T. (1958), "Excretion of Epinephrine and Nor-epinephrine under Stress", *Recent Progr. Hormone Res.*, 14: 513.

FRANKSSON, C., and GEMZELL, C. A. (1955), "Adrenocortical Activity in the Pre-operative Period", *J. clin. Endocr.*, 15: 1069.

FRIEDMAN, M., ROSENMAN, R. H., and CARROLL, V. (1958), "Serum Cholesterol, Blood Clotting and Stress", *Circulation*, 17: 852.

FUNKENSTEIN, D. H., KING, S. H., and DROLETTE, M. (1954), "The Direction of Anger during a Laboratory Stress Inducing Situation", *Psychosom. Med.*, 16: 404.

GERARD, R. W. (1958), "Anxiety and Tension", *Bull. N.Y. Acad. Med.*, 34: 429.

GRACE, W. J., PINSKY, R. H., and WOLFF, H. G. (1954), "Treatment of Ulcerative Colitis", *Gastroenterology*, 26: 462.

GRACE, W. J., and GRAHAM, D. T. (1952), "Relationship of Specific Attitudes and Emotions to Certain Body Diseases", *Psychosom. Med.*, 14: 243.

GRAHAM, D. T., STERN, J. A., and WINOKUR, G. (1958), "Experimental Investigation of the Specificity Attitude Hypothesis in Psychosomatic Disease", *Psychosom. Med.*, 20: 446.

HAM, G. C., ALEXANDER, F., and CARMICHAEL, H. T. (1950), "Dynamic Aspects of the Personality Features and Reactions Characteristic of Patients with Graves' Disease", *Ass. Res. nerv. Dis. Proc.*, 29: 451.

HARRIS, R. E., SOKELOW, M., CARPENTER, L. G., FREEDMAN, M., and HUNT, S. P. (1953), "Response to Psychologic Stress in Persons who are Potentially Hypertensive", *Circulation*, 7: 874.

HETZEL, B. S. (1954), unpublished data.

HETZEL, B. S., SCHOTTSTAEDT, W. W., GRACE, W. J., and WOLFF, H. G. (1955), "Changes in Urinary 17-hydrocorticosteroid Excretion during Stressful Life Experiences in Man", *J. clin. Endocr.*, 15: 1057.

HETZEL, B. S., SCHOTTSTAEDT, W. W., GRACE, W. J., and WOLFF, H. G. (1956), "Changes in Urinary Nitrogen and Electrolyte Excretion during Stressful Life Experiences and their Relation to Thyroid Function", *J. psychosom. Res.*, 1: 177.

HETZEL, B. S., GRACE, W. J., and WOLFF, H. G. (1956), "General Metabolic Changes during Stressful Life Experiences in Man", *J. psychosom. Res.*, 1: 186.

HETZEL, B. S., WILLIAMS, R., and LANDER, H. (1957), "A Comparison of the Early Metabolic Effects of Triiodothyronine and Hydrocortisone in Man", *Aust. Ann. Med.*, 6: 218.

HETZEL, B. S., CHARNOCK, J. S., GILMORE, H., and LEMERCIER, K. (1958), "Alteration in Metabolic Response to Adrenaline by Pretreatment with Triiodothyronine in Man", *Aust. J. exp. Biol. med. Sci.*, 36: 479.

HETZEL, B. S., CHARNOCK, J. S., LAWRENCE, J. R., and WELLBY, M. L. (1960), "Augmentation by Triiodothyronine of Some of the Effects of Hydrocortisone in Man", *Aust. J. exp. Biol. med. Sci.*, in the press.

HETZEL, B. S., BRUER, B., and POIDEVIN, L. O. S. (1959), to be published.

HILL, S. R., GOETZ, F., FOX, H. M., and THORN, G. W. (1956), "Studies on the Adrenal Cortex and Psychological Response to Stress in Man", *A.M.A. Arch. intern. Med.*, 97: 269.

HINKLE, L. E., and WOLF, S. (1952), "Importance of Life Stress in Course and Management of Diabetes Mellitus", *J. Amer. med. Ass.*, 148: 513.

MORRIS, J. N., HEADY, J. A., and BARLEY, R. G. (1953), "Coronary Heart Disease in Medical Practitioners", *Brit. med. J.*, 1: 503.

MOSES, L., DANIELS, G. E., and NICKERSON, J. L. (1956), "Psychogenic Factors in Essential Hypertension: Methodology and Preliminary Report", *Psychosom. Med.*, 18: 471.

PRICE, D. B., THALER, M., and MASON, J. W. (1957), "Pre-operative Emotional States and Adrenal Cortical Activity", *A.M.A. Arch. Neurol. Psychiat.*, 77: 646.

SCHNEIDER, R. A. (1950), "The Relation of Stress to Clotting Time, Relative Viscosity and Certain other Biophysical Alterations of the Blood in the Normotensive and Hypertensive Subject", *Ass. Res. nerv. Dis. Proc.*, 29: 818.

SCHOTTSTAEDT, W. W., GRACE, W. J., and WOLFF, H. G. (1955), "Life Situations, Adaptive Behaviour Patterns, and Renal Excretion of Fluid and Electrolytes", *J. Amer. med. Ass.*, 157: 1485.

SELYE, H. (1936), "A Syndrome Produced by Diverse Nocuous Agents", *Nature (Lond.)*, 138: 32.

SELYE, H. (1950), "Stress", Acta Inc., Montreal.

VENNING, E. H., DYRENFURTH, I., and BECK, J. C. (1957), "Effects of Anxiety upon Aldosterone Excretion in Man", *J. clin. Endocr.*, 17: 1005.

WIENER, H., THALER, M., REISER, M. F., and MIRSKY, I. A. (1957), "Etiology of Duodenal Ulcer: Relation of Specific Psychological Characteristics to Rate of Gastric Secretion (Serum Pepsinogen)", *Psychosom. Med.*, 19: 1.

WOLF, S., and WOLFF, H. G. (1947), "Human Gastric Function: An Experimental Study of a Man and his Stomach", 2nd Edition, Oxford University Press, N.Y.

WOLF, S., CARDON, P. V., SHEPARD, E. M., and WOLFF, H. G. (1955), "Life Stress and Essential Hypertension", Williams and Wilkins, Baltimore.

WOLFF, H. G. (1952), "Stress and Disease", American Lecture Series, Thomas, Springfield, Illinois.

THE INFANT IN CÆSAREAN SECTION.[1]

By KATE CAMPBELL,
Melbourne.

CÆSAREAN SECTION has been studied mainly from the maternal viewpoint. In the present survey the results of the operation have been analysed from the viewpoint of the infant.

Still-birth in Cæsarean section due to the operation itself is so rare that it can be disregarded. Therefore, in estimating the risk to the infant, only the neonatal death rate has been considered. The risk to the infant must be studied from three angles: (i) consideration of the dangers inherent in the operation itself; (ii) the time of the section relative to the time of the rupture of the membranes; (iii) the indication for which the section is performed.

The Hazards of the Operation Itself.

The dangers to the child arise from difficulties in maternal anæsthesia, from fœtal bleeding due to incision of, or trauma to, the placenta or from trauma to the infant.

Maternal Anæsthesia.

Difficulties from maternal anæsthesia may be divided into the following four categories: (i) Maternal cyanosis or hypoxæmia will produce fœtal hypoxæmia, and may result in intrauterine respiration so that the fœtus inhales liquor. (ii) Anæsthesia may be too light, so that the baby breathes too soon after birth to permit adequate sucking out. (iii) Anæsthesia may be too deep, resulting in depression of the infant's respiratory centre with prolonged apnœa at birth. (iv) Certain types of anæsthesia have disadvantages.

The maternal anæsthesia is a most important part of Cæsarean section, and the anæsthetist should have had special training in obstetric anæsthesia.

Placental Hæmorrhage.

Bleeding from the fœtal portion of the placenta is prone to occur in placenta prævia, in which the placenta may be incised before the baby is extracted. This can result in fatal exsanguination of the infant—a condition often mistaken for asphyxia pallida. Points of differentiation are that the exsanguinated infant, though pale, is usually alert, is in a good state of muscle tone and has not a slow pulse, whereas the infant with asphyxia pallida is in a state of shock—unconscious, with poor muscle tone—and has typical bradycardia.

It is wise, in Cæsarean section for placenta prævia, to have in readiness the apparatus for transfusion into the umbilical vein and some group O, Rh-negative blood.

Trauma to the Infant.

Trauma to the infant can occur if the incision in the uterus is too small, or if the presentation is an awkward one. Though rare, intracranial trauma is encountered—most usually a torn tentorium.

If there is very little liquor, the infant may be cut when the uterus is incised.

Cæsarean Section in Relation to Rupture of the Membranes.

The second point to consider is the time of the section relative to the time of rupture of the membranes. This greatly influences the baby's prognosis. It is often difficult to be certain when the membranes have ruptured. In practically all planned Cæsarean sections (elective Cæsarean section) the operation is done before the membranes have ruptured. In the majority of sections carried out during labour, the membranes have ruptured. I have termed section carried out after the onset of labour "obligatory" Cæsarean section.

TABLE I.

Hospital.	Period.	Number of Cases.	Full-Time Births.	Premature Births.	Incidence of Prematurity.
Royal Women's Hospital.	1955–1957	610	546	64	10·5%
Queen Victoria Hospital.	1953–1957	549	482	67	12·2%
Total ..	.. ..	1159	1028	131	11·3%

Elective Cæsarean Section.

In elective Cæsarean section (one done while the membranes are intact), the danger is the hyaline membrane type of atelectasis.

The clinical picture is well known. The infant's condition may be satisfactory for one or more hours after birth. Then, some time within the first 24 hours, there appear sternal retraction, dyspnœa and cyanosis, with intermittent attack of more severe cyanosis. The sternal retraction increases, and in fatal cases the infant dies by the third day. Post-mortem examination reveals the characteristic pulmonary pathological findings, and there is usually increased cerebro-spinal fluid in the sub-arachnoid space.

While there is no unanimity of opinion on the ætiology of this condition, there is no clinical doubt that inhalation of an excessive amount of liquor is necessary for its development. If this is prevented, hyaline membrane atelectasis does not occur. In the ordinary vaginal delivery, the membranes have ruptured and most of the liquor has drained away by the time the head is born. In vertex presentations, the squeezing of the thorax as it passes down the birth canal also aids in ridding the respiratory tract of fluid. In elective Cæsarean section, on the other hand, the infant is extracted from the uterus without any preparation, with his upper respiratory passages full of liquor. Moreover, he is extracted wrong way up with the head uppermost, so that if the handling stimulates respiration he will inhale the liquor.

Since the introduction of what has been termed overseas "the Pash manœuvre", we have practically eliminated hyaline membrane atelectasis in uncomplicated elective Cæsarean operation. Dr. June Pash originated this procedure and described it in 1954. In the series reviewed in this paper, in 175 consecutive elective Cæsarean sections done at the Queen Victoria Hospital for disturbance of mechanism of labour, there were no deaths. The manœuvre consists in aspirating the mouth and pharynx of the infant while the head is still in the uterus. The wound is rendered as dry as possible. The face is brought into the wound, and a No. 7 English size rubber catheter is attached to the sucker. The pædiatrician in attendance is "scrubbed up" as part of the surgical team, and does the sucking. After the infant is extracted he is kept head down, and as this change in position may result in fluid

[1] Read at a meeting of the Section of Medicine, the Section of Obstetrics and Gynæcology and the Section of Pædiatrics, Australasian Medical Congress (B.M.A.), Tenth Session, Hobart, March 1 to 7, 1958.

TABLE II.

Cæsarean Section for Disturbances of Mechanism of Labour.

Type of Delivery.	Royal Women's Hospital.			Queen Victoria Hospital.			Total.		
	Number of Cases.	Deaths.	Mortality Rate.	Number of Cases.	Deaths.	Mortality Rate.	Number of Cases.	Deaths.	Mortality Rate.
Elective.									
Full-time	222	2 (1 hyaline membrane; 1 congenital defect)	0·9%	158	0	0%	380	2	0·52%
Premature	7	2 (1 hyaline membrane; 1 congenital defect)	2 cases out of 7	17	0	0%	24	2	8·3%
Total	229	4	1·7%	175	0	0%	404	4	0·99%[1]
Obligatory.									
Full-time	184	1 (atelectasis)	0·54%	242	1 (congenital defect)	0·41%	426	2	0·46%
Premature	5	0	0%	15	1 (staphylococcal pneumonia—14 days)	1 case out of 15	20	1	5·0%
Total	189	1	0·54%	257	2	0·79%	446	3	0·67%[2]
Grand total	418	5	1·19%	432	2	0·46%	850	7	0·82%
Total, excluding deaths due to congenital defect (3) and staphylococcal pneumonia (1)	416	3	0·72%	430	0	0·00%	846	3	0·35%

[1] Excluding congenital defect, 2 in 402; rate=0·49%.

[2] Excluding congenital defect and staphylococcal pneumonia at 14 days, 1 in 444; rate=0·23%.

TABLE III.

Cæsarean Section for Placenta Prævia.

Type of Delivery.	Royal Women's Hospital.		Queen Victoria Hospital.		Total.	
	Number of Cases.	Deaths.	Number of Cases.	Deaths.	Number of Cases.	Deaths.
Elective.						
Full-time	33	0	35	3 (1 atelectasis; 1 insufflation pneumonia; 1 bronchopneumonia)	68	3
Premature	11	3 (1 hyaline membrane; 1 hyaline membrane and torn tentorium; 1 atelectasis)	13	1 (prematurity)	24	4
Total	44	3	48	4	92	7
Obligatory.						
Full-time	5	0	6	0	11	0
Premature	1	0	4	2 (1 congenital defect; 1 prematurity)	5	2
Total	6	0	10	2	16	2
Grand total	50	3	58	6	108	9
Excluding deaths due to congenital defect ..	50	3	57	5	107	8

TABLE IV.
Cæsarean Section for Accidents to the Cord.

Type of Delivery.	Royal Women's Hospital.		Queen Victoria Hospital.		Total.	
	Number of Cases.	Deaths.	Number of Cases.	Deaths.	Number of Cases.	Deaths.
Elective.						
Full-time	10	0	12	1 (insufflation pneumonia)	22	1
Premature	6	4 (1 atelectasis and pneumonia; 1 atelectasis; 1 hyaline membrane; 1 hyaline membrane and pneumonia)	2	1 (hyaline membrane)	8	5
Total	16	4	14	2	30	6
Obligatory.						
Full-time	19	0	6	0	25	0
Premature	6	0	4	0	10	0
Total	25	0	10	0	35	0
Grand total	41	4	24	2	65	6

running into his pharynx, this is again sucked out. Because handling of the nostrils stimulates respiration, the nose is not sucked out at this stage. Clamping of the cord stimulates the baby to breathe, and is therefore delayed till the sucking out is completed. The sucking out is done at the operation table, and the infant is then transferred—still in the head-down position—to the resuscitation cot or bench and kept with the head below the chest. When the pharynx has been cleared, the nose can be sucked out.

If the baby is slow to breathe, oxygen can be given by intranasal catheter or, more effectively, by Åkerren's intragastric method. When the baby is breathing satisfactorily, the stomach is aspirated (unless it has been previously aspirated, if oxygen has been given by Åkerren's method).

In the case of a breech birth the manœuvre is not possible. It is advisable in these cases to make a small incision in the uterus to allow the liquor to drain away before making the usual incision.

It is my impression that infants who inhale blood as well as liquor do very badly. I have attributed this to the thromboplastic effect of the liquor on the inhaled blood.

In executing this simple manœuvre, the cooperation of the anæsthetist is important. It is desirable that the baby should not breathe immediately he is born, so as to permit time for further sucking out. The appropriate grade of anæsthesia and the avoidance of fœtal hypoxæmia are of great assistance in bringing this about. An interval of one to two minutes is helpful.

The Obligatory Cæsarean Section.

In most cases of obligatory Cæsarean section the membranes have ruptured. The risks to the infant are (i) anoxia, (ii) trauma and (iii) infection; they are risks from the abnormal labour, not from the Cæsarean section.

If the membranes are intact at the time of operation, there is the risk of hyaline membrane atelectasis.

The Indication for Cæsarean Section.

The third consideration is the indication for which the section is performed. This has a powerful effect on the prognosis.

The indications for Cæsarean section may be divided into the following five main groups: (i) distrbances of the

TABLE V.
Cæsarean Section for Toxæmia (including Hypertension).

Type of Delivery.	Royal Women's Hospital.		Queen Victoria Hospital.		Total.	
	Number of Cases.	Deaths.	Number of Cases.	Deaths.	Number of Cases.	Deaths.
Elective.						
Full-time	13	0	7	1 (atelectasis and congenital defect)	20	1
Premature	17	4 (2 hyaline membrane; 1 atelectasis; 1 undetermined)	8	2 (1 prematurity; 1 anoxia)	25	6
Total	30	4	15	3	45	7
Obligatory.						
Full-time	1	0	3	—	4	—
Premature	3	0	—	—	3	—
Total	4	0	3	—	7	—
Grand total	34	4	18	3	52	7

mechanism of labour; (ii) placenta prævia; (iii) accidents to the cord; (iv) toxæmia; (v) miscellaneous, including (*a*) maternal diabetes, (*b*) placental insufficiency, (*c*) a bad previous obstetric history, (*d*) medical indications and (*e*) fœtal erythroblastosis with previous bad history.

The Present Series.

In order to estimate the risks to the child, I have analysed the neonatal deaths in a consecutive series of

TABLE VI.

Indication for Cæsarean Section.	Number of Cases.	Deaths.
Diabetes	54	4
Placental insufficiency	15	0
Previous bad obstetric history	6	0
Medical indication	8	0
Fœtal erythroblastosis with history of previous intrauterine deaths	1	1

booked ante-natal cases in the two public midwifery hospitals in Melbourne, taking infants of a birth weight of 2 lb. (900 grammes) and over for the period 1953-1957. I have taken two hospitals, so as to equalize different approaches to Cæsarean section.

It will be seen from Table I that the incidence of prematurity in the series is 11·3%—higher than that usually found, 6%—so that the mortality rate is loaded a little as compared with an average cross section of births.

The cases are divided into five groups according to the indication. Cæsarean section undertaken before the onset of labour is designated "elective", and that performed after the onset of labour as "obligatory". This is as near as I could get to the question of section before or after rupture of the membranes.

Each series of infants is divided into full-time and premature, the international standard weight of 5 lb. 8 oz. (2500 grammes) and less being taken as the definition of prematurity.

The usual anæsthesia employed was "Pentothal" induction (with or without "Flaxedil"), nitrous oxide and oxygen, and in special instances, ether.

Disturbances of the Mechanism of Labour.

Disturbances of the mechanism of labour (Table II) included those cases in which the section was done for some mechanical cause which prevented safe vaginal delivery—for example, contracted pelvis, disproportion, abnormal presentation, disordered uterine action, etc.

The interesting thing about this series is the very low neonatal death rate. There were seven deaths among 850 infants, an over-all mortality rate of 0·83%. Three of these deaths were due to congenital malformation, and one infant died of staphylococcal pneumonia at the age of two weeks. If these are excluded, there are left three deaths among 846 live-born infants, all due to atelectasis—that is, a mortality rate due to the operation of 0·35%.

This group gives the clearest picture of the risks of the operation, as by and large the mothers were in normal health, and there were no other obstetric difficulties present to complicate the result of section.

From these figures—particularly those of the hospital in which 430 sections were carried out without any neonatal loss from the operation itself—we can deduce that, in competent hands, the risk to the infant from the operation of Cæsarean section is minimal.

Placenta Prævia.

The risks to the fœtus in placenta prævia (Table III) are as follows:

1. Anoxia from maternal blood loss. This, if not gross, may produce intrauterine respiration, with inhalation of liquor and possibly blood. This will cause either primary obstructive atelectasis at birth, or later the hyaline type of atelectasis. If it is severe, the infant will be still-born.

2. Exsanguination from tearing or incision of the fœtal portion of the placenta.

3. Prematurity. This greatly impairs the infant's prognosis. Most obstetricians now carry the pregnancy as late as is compatible with safety.

TABLE VII.

Cæsarean Section for Miscellaneous Indications.

Type of Delivery.	Royal Women's Hospital.			Queen Victoria Hospital.			Total.	
	Indication for Cæsarean Section.	Number of Cases.	Deaths.	Indication for Cæsarean Section.	Number of Cases.	Deaths.	Number of Cases.	Deaths.
Elective.								
Full-time	Diabetes	37	2 (hyaline membrane)	Diabetes	6			
				Medical reasons	4	11	0	65	2
	Placental insufficiency	9 (54)	—	Fœtal erythroblastosis	1			
	Poor previous obstetric history	5	—					
	Medical reasons	3	—					
Premature	Diabetes	5	1 (hyaline membrane)	Diabetes	4	1 (congenital defect)	—	—
	Placental insufficiency	1 (8)	—				12	2
	Poor previous obstetric history	1	—					
	Medical reasons	1	—					
Total		62	3		15	1	77	4
Obligatory.								
Full-time	Placental insufficiency	5	0	Diabetes	2	0	7	0
Premature		0	0		0	0	0	0
Total		5	0		2	0	7	0
Grand total		67	3		17	1	84	4

The actual operation risk in this condition is that of bleeding from the incised placenta, which was considered earlier.

In this series there were 108 cases with nine deaths. It comprised 79 full-time infants with three deaths, and 29 premature infants with six deaths. Of the nine deaths, one was due to hyaline membrane atelectasis, one to hyaline membrane atelectasis complicated by a torn tentorium, two were due to ordinary atelectasis and two to insufflation bronchopneumonia, probably due to the inhaled blood. Two are described as due to prematurity, which probably indicates anoxia, as no other pathological cause was found. One was due to congenital defects.

The outcome in placenta prævia is so dependent on the causative condition that it is difficult to evaluate the position of Cæsarean section without studying the question as a whole. The contribution the pædiatrician can make is to stress the danger of bleeding from the incised placenta and the advisability of having blood and apparatus ready for an umbilical vein transfusion.

TABLE VIII.

The Mortality in the Different Groups.	Number of Cases.	Rate.
Disturbance of mechanism of labour	850	0·82%
Placenta prævia	108	8·3%
Accidents to the cord	65	6 deaths
Toxæmia and hypertension	52	7 deaths
Miscellaneous	84	4 deaths

Accidents to the Cord.

Again in accidents to the cord (Table IV), the neonatal death rate gives only part of the picture, many infants being still-born. From this series, however, it was clear that the risk was much less when prolapse occurred during labour than when it occurred before the onset of labour. This may be due to the fact that earlier recognition of the accident is more likely during labour.

There were no deaths in 36 cases of prolapsed cord occurring during labour, whereas the mortality was six in 28 cases in which the accident occurred before the onset of labour. In this latter group the risk was particularly great to the premature infants; five out of eight died, all from atelectasis.

Toxæmia and Hypertension.

The cases of toxæmia and hypertension (Table V) formed the smallest group, and the one with the highest mortality. There were no deaths among the few cases in which Cæsarean section was performed during labour, and only one full-time infant died out of the 20 full-time infants delivered by elective Cæsarean section; this was an infant with congenital defect and atelectasis. The mortality was highest among the premature infants delivered by elective Cæsarean section—six out of 25 cases, three deaths being due to atelectasis.

Miscellaneous.

The miscellaneous group included those cases in which the indication was as set out in Table VI. The results are seen in Table VII. It is in this group that collaboration between obstetrician, physician and pædiatrician is essential.

Summary.

The over-all mortality rate in the whole series of 1159 cases was 33 (2·85%), the mortality rate for the full-time infants (1028) was 11 (1·07%), and for the premature infants (131), 22 (16·8%). The mortality in the different groups is seen in Table VIII.

I have compared these findings, in Table IX, with the average neonatal death rate among live-born infants of booked patients at the two hospitals over the periods under review. The results are not quite comparable, as the hospital statistics have taken a birth weight of 2 lb. 12 oz. (1250 grammes) as the pre-viable level, and I have taken a birth weight of 2 lb. (900 grammes), which again gives a loading against the series reviewed.

As was pointed out earlier, it is the "disturbed mechanism of labour" group which gives the truest picture of the operation risk. It was practically the same as the general neonatal death rate obtaining in both hospitals—actually a little better.

TABLE IX.

Hospital.	Number of Cæsarean Sections.	Number of Deaths.	Mortality Rate. (Percentage.)	Average Hospital Neonatal Mortality Rate for Period under Review.
Royal Women's Hospital ..	610	19	3·11	0·9%
Queen Victoria Hospital	549	14	2·55	0·9%

Conclusion.

From a pædiatric survey of the results of Cæsarean section in Melbourne over the period 1953-1957, the conclusion is reached that the operation, in competent hands and with skilled anæsthesia, is a safe method of birth for the child, the neonatal death rate attributable to the operation being 0·35%.

When other complications exist, either obstetric or medical, the neonatal mortality depends almost entirely on the outcome of the complication.

Reference.

PASH, J. (1954), "Prevention of Hyaline Membrane after Cæsarean Section", MED. J. AUST., 2: 386.

SOCIAL INFLUENCES IN HEALTH AND DISEASE.[1]

By HENRY SHANNON,
Melbourne.

A physician observing a disease in different circumstances, reasoning about the influence of these circumstances, and deducing consequences which are controlled by other observations,—this physician reasons experimentally, even though he makes no experiments.

—CLAUDE BERNARD.

THE medical and teaching professions are met here to consider in what ways they can best combine their efforts in order to improve the health of children and, as we shall see, that of the adult population as well. It will be necessary to pose a number of questions to ourselves; some of them will be at high-policy level verging upon the fields of statecraft, and others, no less difficult to answer, will emerge from the technical problems of medicine and education.

I should be breaking a long-established tradition if I did not commence my discourse with a definition of health, and I know of none better than that of the World Health Organization, which is "physical, mental and social well-being". Most of us feel that we can recognize positive health when we encounter it, and are content to call it "satisfactory adaptation of the individual to his environment within the limits of his inherited endowments".

For this audience I will not attempt a definition of education; but one for health education may not be out

[1] A version of the opening paper read at a residential seminar in Melbourne in May, 1959, for principals of teachers' colleges, educational psychologists, physical educationists and school medical officers.

of place. We believe it to be an attempt, at an intellectual level, to persuade people to alter their present patterns of living to more healthy ones.

There have been remarkable improvements in the state of the public health in the last half-century, and a day could be spent in analysing the factors which have contributed to the change. One very notable example is provided by the decline in the incidence and mortality from bowel diseases, as shown in Figure I. In this case, the abrupt fall coincided with the introduction of water-borne sewage, and since this experience can be matched all

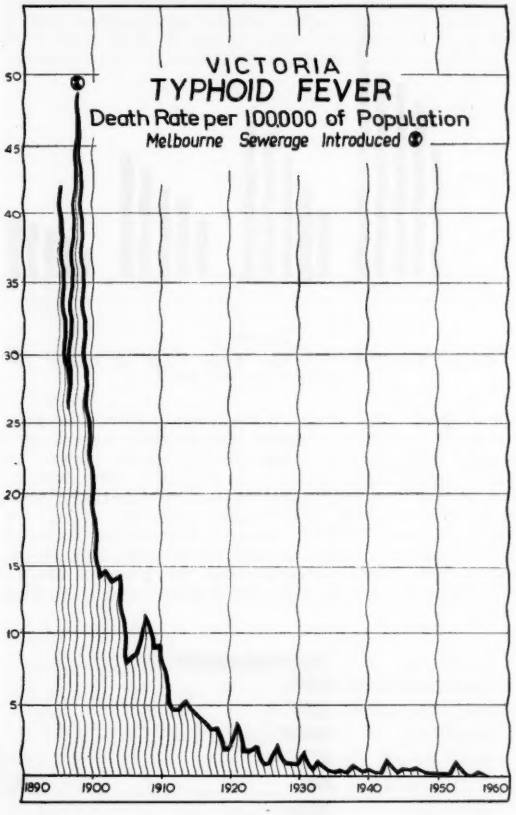

FIGURE I.

Victoria: typhoid fever; death rate per 100,000 of population. (Figures from the Government Statist.)

over the world we are entitled to believe that the conjunction is a real one. To give effect to it, it was necessary only to create a Melbourne and Metropolitan Board of Works and give it certain powers of regulation. No educational programme was necessary to make the new system function; the Board spoke and it was done.

If we turn from this to another ancient scourge of mankind, tuberculosis, we can discern a mixture of factors at work in reducing the incidence. Here progress was slow until government action provided the means for early detection and segregation of patients. Adequate pension rates permitted sources of further infection to isolate themselves, and technical advances in their treatment may see the extinction of the disease. No single one of these measures alone would have sufficed; first our leaders had to have a clear perception of the problem, and then the public had to understand fully the modes of propagation of the disease and the minute details of hygiene within the home and elsewhere which would control it. In other words, health education played an important part.

Infant mortality will take us a stage further in our inquiry. In Figure III we see the extraordinary changes that have occurred in half an ordinary lifetime; but in spite of these improvements there still remains a marked difference between the social classes. Here again we see a mixture of social and economic factors at work. However, those who are intimately familiar with this field of prevention will agree without question that health education dominated all others (see Figure IV). From Truby

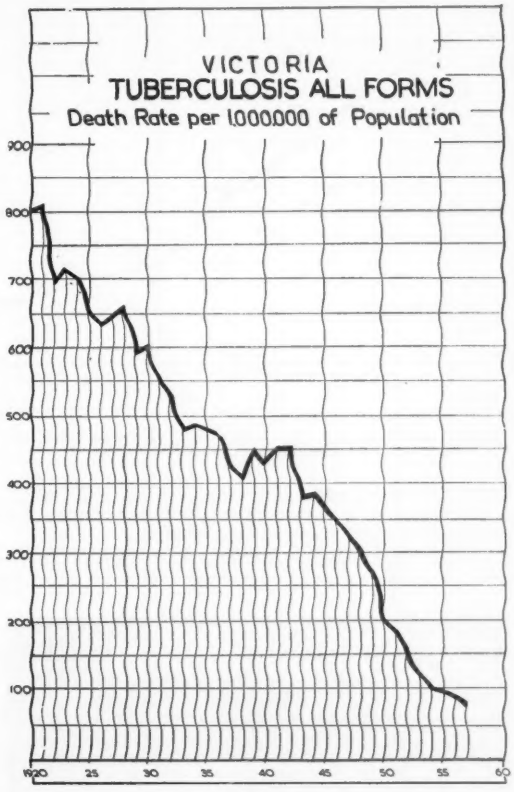

FIGURE II.

Victoria: tuberculosis, all forms; death rate per 100,000 of population. (Figures from the Government Statist.)

King and others through a long line of infant welfare workers, an intensive campaign of education passed like a tidal wave around the world. One factor would be a nurse slowly persuading a mother to measure the ingredients of an artificial feed, another an interview devoted to the hygiene of the mouth or skin; yet another would be instruction in altering the physical environment or in changing the emotional climate of the home. At no time and nowhere could government action have accomplished any of these tasks.

The five social classes of the Registrar-General are as follows: I, professional; II, intermediate; III, skilled tradesman; IV, intermediate; V, unskilled labourer. In the graph in Figure V, we may observe that the infant mortality rate in the family of the unskilled labourer of today is lower than that enjoyed by the barrister's family of 1920. The improvement lies in the education of mothers, who, armed with knowledge, are able to combat successfully the defects of their infants' environment. Those of us who have practised family medicine will recall an occasional but outstanding home in a row of poor

dwellings. The mother has been educated to a standard *noticeably higher than that of her neighbours; on an* income no higher and in an environment no different, she succeeds in rearing a better and healthier family than *her neighbours. There can be no doubt that education* and health education are the dominating factors.

In a general review of the falling trends of incidence of infectious disease, it may be argued that humanity is undergoing a widespread form of physical evolution, in the course of which, by urbanization and other factors, it is acquiring a higher resistance; there is little evidence *to support this view and much against it.*

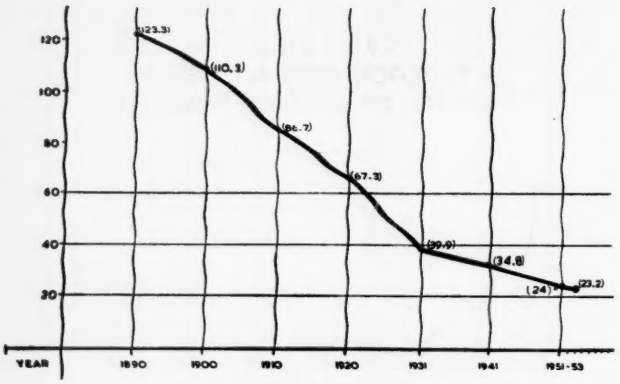

FIGURE III.
Infant mortality rate in Australia. (Figures from the Government Statist.)

If we turn from physical evolution to cultural evolution, we may perceive a darker picture. I will confine myself to quoting no more than three examples.

Violence far overshadows all other causes of death among Australian boys up to the age of 14 years; drowning,

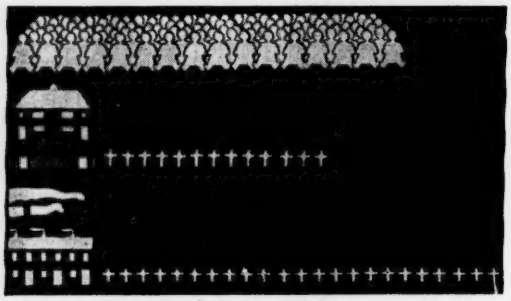

FIGURE IV.
Infant deaths per 1000 births in two areas of London.

poisoning, burning, electrocution and transport accidents are all in varying ways and degrees expressions of ignorance and even of want of moral standards. Government can do little more and a wide field for careful and continuing education is open.

The evidence which incriminates excessive cigarette smoking as a factor in causing lung cancer is irrefutable. Government prohibition is unlikely, and the solution can be only an educational one; teachers and doctors must soon decide what part they are to play in it.

Finally, coronary disease must have some mention. In Greater Melbourne in 1957, 15,000 people died, and of this number 3200 perished from this form of heart disease. Later in the seminar, I hope that one of us may present to the teaching profession an analysis of the evidence by *which we are led to believe that it is a new epidemic,* and that it arises out of cultural changes. From the discussion which should follow, one would hope—optimistically, *perhaps—that an educational programme to combat it* might be evolved.

In the time available, I cannot hope to do justice to the fundamental changes in approach to prevention which changing patterns of living are bringing to light.

In a wider sphere, but of no less urgent need, the situation resembles that which arose during the second

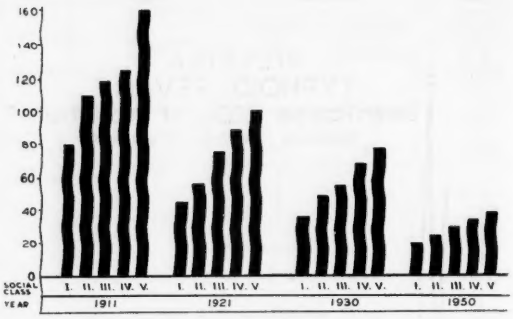

FIGURE V.
Infant mortality rate by social class of father (for explanation see text).

World War. The sanitary regulations slowly adopted by the army from the Crimean war onwards served us well enough until jungle warfare in the tropics began. From then on, each man was on his own; his own care of his person, his own individual malaria precautions, his own moral fibre—indeed, his "health education status"—were *vital to success. Without these, no army order, no technical* instruction, no equipment medical or otherwise served its full purpose. Self-discipline took the place of discipline, and education was its root and branch; and so it must be again.

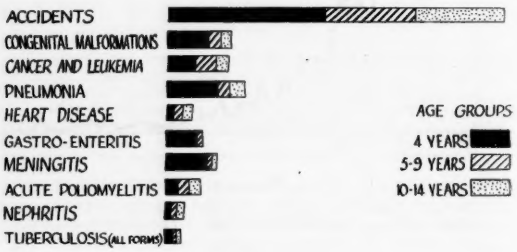

FIGURE VI.
Death rates of Australian male children.

In the present campaign there are two professions that must play a leading role, and the reasons are few but compelling. The medical profession has the knowledge to convey and the prestige to hold the public attention. It must learn to present the subject competently and persuasively. The teaching profession is skilled in the arts of communication and has a vast audience—present by compulsion, and for a long time. This audience is made up of children, whose minds are impressionable and whose habits and attitudes are not yet fixed by long usage. It is the main business of this seminar to discover how best the first profession can communicate with the second and that one in turn with the school population.

I cannot leave the subject of the respective roles of teacher and doctor without reminding the doctors that,

throughout their bedside practice, their words of advice and their explanations of cause and effect have been understood by their patients only because these patients were once children in a State school and learned something of their bodies' workings there. This fact goes almost entirely unrecognized by the medical profession at large.

In case someone is not yet satisfied with the proofs which I have provided that environment is an important factor in health and disease, and that education is an equally important one in combating it, I should like to pursue the argument a stage further.

Of course, no great perspicacity is required to decide that the environment of the school of 1900 was less healthy than that of one of 1950. In the old one, four out of every ten girls had lice in their heads, in the new school perhaps one in 100 only. In the histories of the children in the old schools, one would find in a family of five or six a death from whooping-cough in infancy, a case of diphtheria or one of scarlet fever with severe complications. On the other hand, there was a rich family life—a mother always near the kitchen and a feeling of cohesiveness and stability in marked contrast to the present. Reminding ourselves that health depends upon physical and mental as well as on social factors, we begin to recognize whither health education must now be redirected, and where new emphasis must be laid.

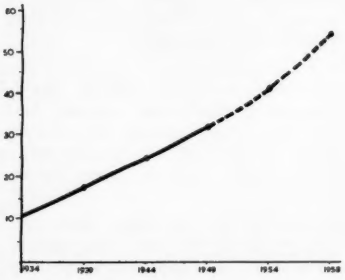

FIGURE VIII.

Victoria: death rates per 10,000 in males aged over 35 years, from coronary diseases, etc. (solid line), and from arteriosclerotic heart disease (interrupted line). (Figures from the Government Statist.)

In attempting to unravel the environmental factors which contribute to health and disease, we have at our disposal a variety of important statistical studies. Theoretically at least, the most reliable one should be the study of identical twins who had been reared apart; but in the upshot not a great deal has been added to our precise knowledge of the relative importance of nature versus nurture in twin studies. Indeed, it has been said that "what nature can do nurture can do equally well", and this view accords fairly closely with our experience of children taken from one environment in infancy and adopted into another.

Another and more fruitful source of information is the study of the health experience of the different social

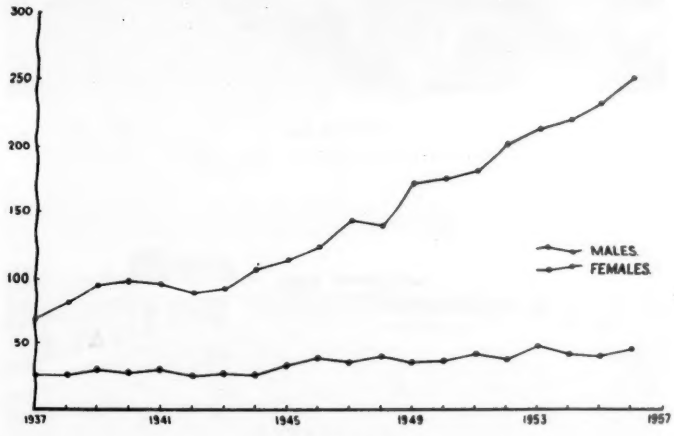

FIGURE VII.

Australia, 1937-1956: death rate from respiratory cancer per 1,000,000 per year, all ages.

classes; the weakness here, of course, is that we have to assume that the members of these socio-economic groups all have similar hereditary endowments, and this may not be true.

The simplest study in this connexion can be taken from the industrial field. For example, a worker in a car-battery factory is some thousands of times more likely to suffer from lead poisoning than is a worker in almost any other kind of industry; and to underline the point again, a battery worker who has been taught industrial hygiene is far less likely to suffer lead poisoning than is a recent and uninstructed recruit to the industry.

When we come to consider some other common causes of ill health, it becomes increasingly difficult, but not impossible, to estimate the importance of education in their prevention. With such conditions as duodenal ulcer, coronary disease or dental caries, all of which have shown rapid increases and have a strong social bias, it must be assumed that the underlying factors are a complex of cultural changes and as such are perfectly susceptible to remedy by education.

So far all my remarks have been directed to sustaining the view that the future of preventive medicine will be different from the past, and that the most powerful instrument in effecting its aims will be health education. The school teacher who is destined to play the dominant role has other tasks in health as well. It is his statutory duty to recognize and report as early as possible the presence of infectious disease in his class and take appropriate steps; in addition, he must be watchful for physical defect, mental abnormality, social maladjustment and other departures from normality. He must know when to intervene and when not to, be versed in the

channels through which to direct those in need of care, and withal be adept in the technique of the teacher-parent interview. He must be knowledgeable in sanitary law and practice in order to maintain the physical standards of the school building, and finally, but most important of all, he must be informed in the maintenance of his own health.

FIGURE IX.
Typical school interior, about 1900.

FIGURE X.
Typical modern school.

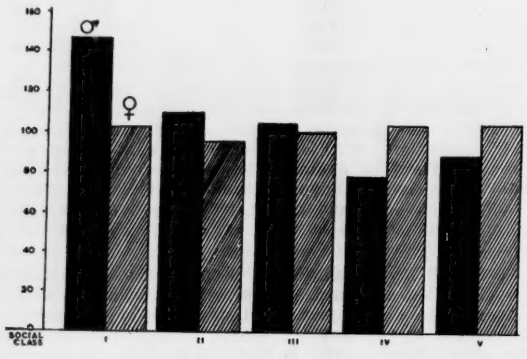

FIGURE XI.
Standardized mortality ratios, coronary disease. (Figures from the Government Statist.)

There appears to be a growing demand in the colleges for education by which students may learn to grapple with those instinctual drives which often disturb them.

This seminar will, one hopes, devote a great deal of time to deciding what and how much of each of these important subjects should be taught. Much new light is being thrown on the problems of juvenile delinquency and of alcoholism, and on another serious problem—the social rejection and withdrawal of the migrant. Should these subjects be presented to student teachers? I believe so, unless we are to reap the bitter harvest that the United States has reaped over the years.

No reference has been made to methods of presentation either in the colleges or in the schools, but I believe that doctors and teachers can learn a great deal from each other. Woven into the problems of presentation is the all-important one of motivation. In this field particularly, doctors have a great deal to learn from educational psychologists.

To summarize then: a wide field of educational endeavour is opening to us all. We should try to find Australian answers to Australian problems, turning abroad only to mark the physical and social disorders which have occurred in countries more advanced than ourselves on the road to environmental and cultural change. We want to know in detail what to teach and how to teach it, and how best to organize and prepare ourselves for the work.

Acknowledgement.

This paper is published by permission of Dr. Kevin Brennan, Chief Health Officer, Department of Health, Victoria.

ILLUSTRATION TO THE ARTICLE BY ERIC V. MACKAY.

FIGURE I.

Centrilobular zone of liver, showing slightly disordered liver-cell trabeculæ, a few bile thrombi, some bile staining of liver cells and mild cellular infiltration. There is also evidence of increased regenerative activity. (× 400.)

ILLUSTRATIONS TO THE ARTICLE BY J. M. HANDLEY.

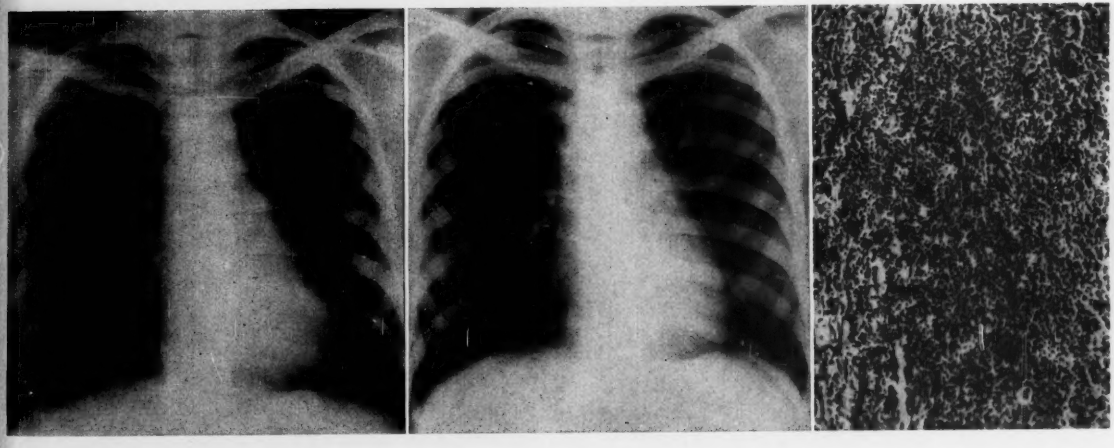

FIGURE I.—Female patient, aged 15 years, with prolonged pyrexia defying diagnosis. Normal skiagram taken on admission to hospital during the sixth month of the illness. FIGURE II.—Six weeks after admission to hospital, showing widening of the upper mediastinal shadow. This led to scalene node biopsy. FIGURE III.—Scalene node biopsy seven weeks after admission to hospital, showing increased hyaline reticulum, diffuse lymphocytic arrangement in the medulla, and giant cells with irregular or multiple darkly-staining nuclei. This established the diagnosis of Hodgkin's disease. (Hæmatoxylin and eosin stain, × 96.)

ILLUSTRATIONS TO THE ARTICLE BY L. F. MASEL.

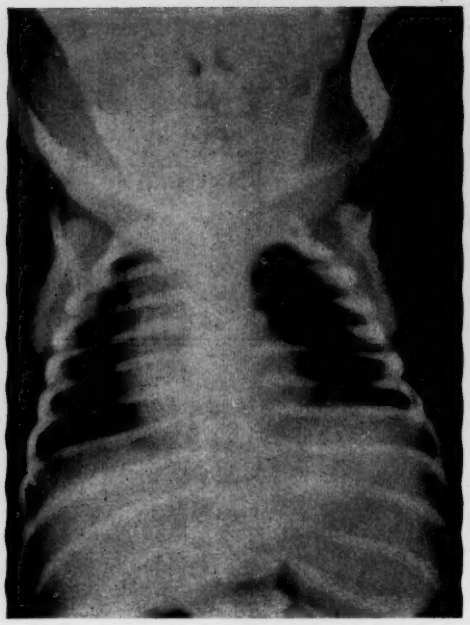

FIGURE I.
X-ray film of the chest, June 16, 1958.

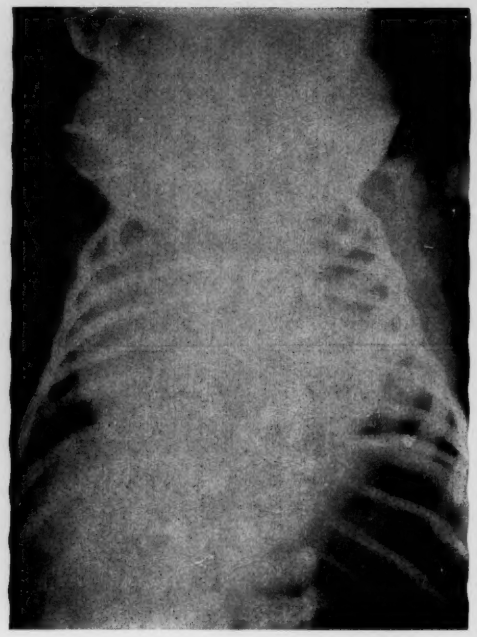

FIGURE II.
X-ray film of the chest, July 9, 1958.

ILLUSTRATIONS TO THE ARTICLE BY J. W. GRAHAM.

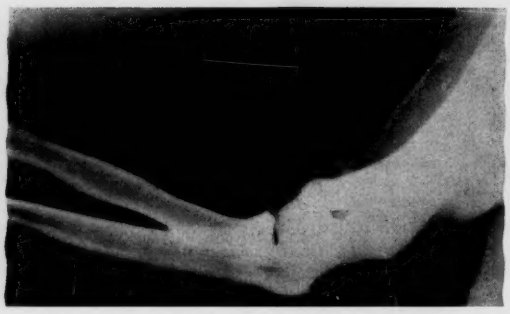

FIGURE IA.
Arteriogram of vein graft one week after insertion.

FIGURE IB.
Arteriogram of vein graft five weeks after insertion.

SERUM HEXOSAMINE LEVEL IN THE DIAGNOSIS OF HODGKIN'S DISEASE.

By S. WEIDEN,[1]

From the Clinical Research Unit of the Walter and Eliza Hall Institute of Medical Research and the Royal Melbourne Hospital, Melbourne.

IN a previous paper (Weiden, 1958), it was shown that patients with Hodgkin's disease had serum hexosamine values higher than in normal persons used as controls, or in patients suffering from a number of other pathological conditions. This led to the claim that estimation of the serum hexosamine level would be of value in diagnosing Hodgkin's disease.

This finding was first brought to my notice in the investigation of a male patient, aged 24 years, with pyrexia of undetermined cause which did not respond to antibotics. Unfortunately the significance of the greatly elevated serum hexosamine level of 229 mg. per 100 ml. (normal range, 80 to 124 mg. per 100 ml.) was not then appreciated. The patient died before the correct diagnosis was made, a post-mortem examination revealing Hodgkin's disease. In the present issue of this Journal (page 212) Dr. J. Handley reports a further case of Hodgkin's disease in which the patient exhibited sustained pyrexia. This case at first defied diagnosis, but later a high serum level of hexosamine, a slowly expanding mediastinal shadow on serial X-ray examinations, and finally a scalene node biopsy led to the correct diagnosis and successful treatment.

Method of Estimating the Serum Hexosamine Level.

The patients were not fasted prior to being tested, as it had been shown that food had no effect on the serum hexosamine level (Weiden, 1958). The test was carried out as follows:

One millilitre of 4N hydrochloric acid was added to 1 ml. of the patient's serum, and the sample was hydrolysed in a boiling water bath for six hours. After being cooled it was neutralized to pH 6·5 with 4N caustic soda solution, and made up to a final volume of 20 ml. with water and filtered. The hexosamine content of 1 ml. of the filtrate was then determined by Weiden's modification of the method of Elson and Morgan (Weiden, 1958; Elson and Morgan, 1933).

Results.

The serum hexosamine levels in normal subjects and in patients with a number of pathological conditions are shown in Figure I. The range for serum hexosamine level in normal subjects was found to be 80 to 124 mg. per 100 ml., with a mean value of 101·5 mg. per 100 ml. $\mp$ 11 mg. per 100 ml. (Weiden, 1958).

Serum was obtained from six patients with untreated Hodgkin's disease, and very high values were obtained from five—200, 210, 228, 229 and 260 mg. per 100 ml. respectively; the remaining patient had a raised value of 148 mg. per 100 ml. The first patient of the six (with the level of 200 mg. per 100 ml.) is the one whose case is described by Dr. J. Handley in this issue. This patient was given 4 mg. of nitrogen mustard intravenously, and this was followed by five similar doses at two-day intervals. Five days after the beginning of therapy, the serum hexosamine level was 220 mg. per 100 ml., but by the twenty-fifth day the level showed a most gratifying fall to a normal level—124 mg. per 100 ml. (Figure II). Moreover, the patient's condition was much improved, with subsidence of the pyrexia, shrinkage of the mediastinal shadow and control of the anæmia. Four months later (April, 1959), the hexosamine level was being maintained within the normal range (133 mg. per 100 ml.).

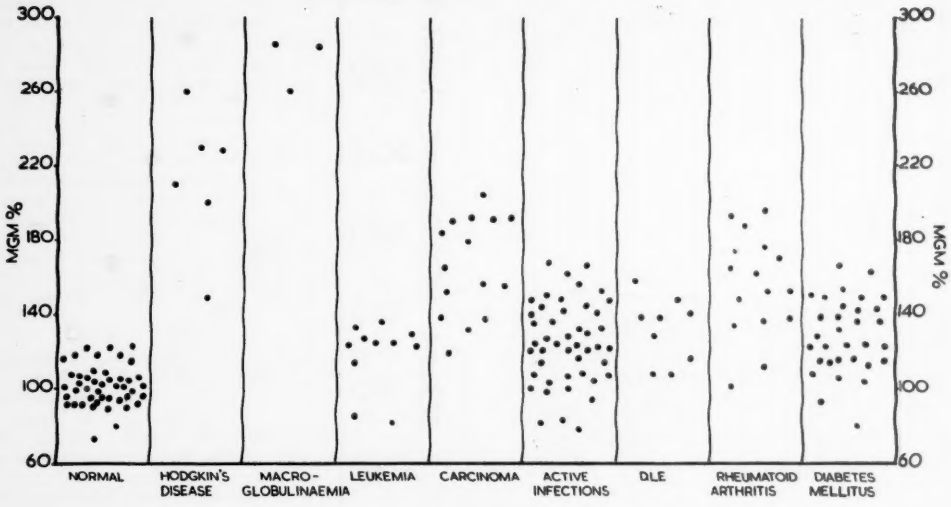

FIGURE I.
Serum hexosamine levels in normal and pathological conditions, including cases of untreated Hodgkin's disease.

The serum hexosamine levels in eight cases of treated and six other cases of untreated Hodgkin's disease are shown in Figure III; the treated patients gave significantly lower values.

Discussion.

Hexosamines have been shown to be present in the ground substance of connective tissue as components of mucopolysaccharides and mucoproteins (Meyer, 1938; Meyer and Rapport, 1951; Consden *et alii*, 1953). In those conditions associated with excess proliferation and breakdown of tissue, there probably occur a shedding of the breakdown products into the tissue spaces and absorption into the blood stream, with a resulting rise in the serum hexosamine level.

Patchy necrosis of cells is a characteristic feature of Hodgkin's disease and could account for the high serum levels of hexosamine. It is accompanied by considerable

[1]Working with the aid of a grant from the National Health and Medical Research Council of Australia.

proliferation of cells, accumulation of reticulum and eventual fibrosis.

In carcinoma there is an increased production of tumour and its stroma at the expense of the body tissues. This continuing erratic growth of the tumour is accompanied from time to time by excess cell necrosis. As a result, much cellular material may be rapidly thrown into the metabolic pool, with elevation of the serum hexosamine level.

Increased synthesis of mucopolysaccharides in the ground substance of connective tissue in rheumatoid arthritis could account for the moderately high serum hexosamine values obtained in this disease.

The serum hexosamine level was moderately raised in active infections such as acute rheumatic fever and

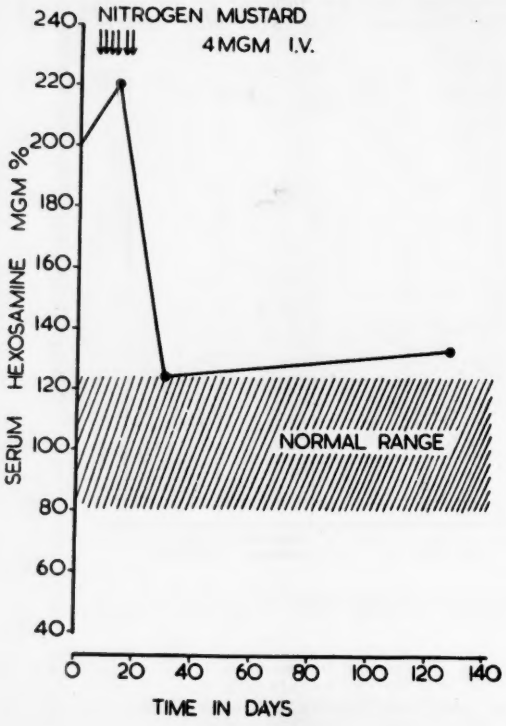

FIGURE II.

Effect of treatment on serum hexosamine level in Hodgkin's disease.

pneumonia. This increase has been shown to be due to an increase in the hexosamine content of the globulins, particularly the alpha-1-globulin (Nilsson, 1937; Bollett *et alii*, 1957).

The very high hexosamine values found in the three cases of macroglobulinæmia can be accounted for by the excessive synthesis of abnormal serum globulins of high molecular weight (Mackay *et alii*, 1956).

In conclusion, it may be stated that a high serum level of hexosamine may be found in a variety of diseases, and it reflects either a fundamental histochemical response to injury or excess tissue proliferation and breakdown.

The finding of very high serum values of hexosamine in untreated Hodgkin's disease may be of considerable value in differentiating this disease from the chronic infections and other conditions, such as leukæmia, which may present a problem in diagnosis.

Summary.

1. The normal serum level of hexosamine has been found to be 80 to 124 mg. per 100 ml., with a mean value of 101·5 mg. per 100 ml. ± 11 mg. per 100 ml.

2. Patients with active infections have been shown to have normal or only moderately elevated serum hexosamine levels.

3. High values were obtained in cases of rheumatoid arthritis, carcinoma and macroglobulinæmia.

4. The serum hexosamine level in five of six patients with untreated Hodgkin's disease was found to be considerably elevated, being over 200 mg. per 100 ml.

5. A case of Hodgkin's disease is described in which the serum hexosamine level fell from 200 mg. to 124 mg. per 100 ml. after the administration of nitrogen mustard. Dr. J. Handley gives a detailed account of this case on page 212 of this issue.

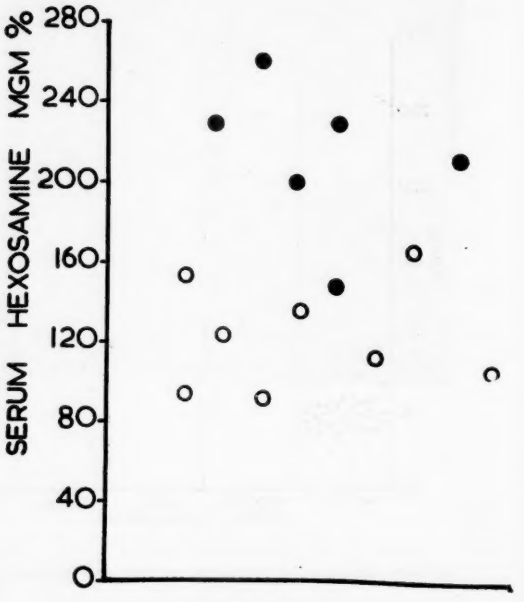

FIGURE III.

Serum hexosamine levels in cases of treated and untreated Hodgkin's disease. Open circles, treated patients; solid circles, untreated patients.

6. It is submitted that the estimation of the serum hexosamine level may be a valuable aid in the diagnosis of Hodgkin's disease.

Acknowledgements.

My thanks are due to Dr. Clive Fitts for kindly allowing me to study one of the cases in this paper. I also wish to thank the other members of the Clinical Research Unit for their help.

References.

BOLLETT, A. J., ROZHIN, J., and SIMPSON, W. (1957), "The Hexosamine Content of the Serum Globulins in Normal and Pathological Sera", *J. clin. Invest.*, 36: 51.

CONSDEN, R., GLYNN, L. E., and STANIER, W. M. (1953), "The Chemical Examination of Connective Tissue in Rheumatic Fever", *Biochem. J.*, 55: 249.

ELSON, L. A., and MORGAN, W. T. J. (1933), "A Colorimetric Method for the Determination of Glucosamine and Chondrosamine", *Biochem. J.*, 27: 1824.

HANDLEY, J. N. (1959), "Scalene Node Biopsy in the Diagnosis of Pyrexia of Unknown Origin", MED. J. AUST., 1: 212.

MACKAY, I. R., ERIKSON, N. MOTULSKI, A. G., and VOLWILER, W. (1956), "Cryo- and Macroglobulinæmia: Electrophoretic Ultracentrifugal and Clinical Studies", *Amer. J. Med.*, 20: 564.

MEYER, K. (1938), "The Chemistry and Biology of Mucopolysaccharides and Glycoproteins", *Cold Spr. Har. Symp. quant. Biol.*, 6: 91.
MEYER, K., and RAPPORT, M. A. (1951), "The Mucopolysaccharides of Ground Substance of Connective Tissue", *Science*, 113: 596.
NILSSON, I. (1937), *"Über den Glucosamingehalt des Blutserums bei Gesunder und Pneumoniekranken"*, *Biochem. Z.*, 290-291: 254.
WEIDEN, S. (1958), "Serum Hexosamine Levels in Health and Disease", *J. clin. Path.*, 11: 177.

THE USE OF HALOTHANE–NITROUS OXIDE FOR OUT-PATIENT DENTAL WORK.

By W. H. J. COLE, D.A., F.F.A.R.A.C.S.,
Melbourne.

OVER the last ten to fifteen years, the practice of dentistry in relation to general anæsthesia has changed, in that extraction of teeth, tooth roots and unerupted teeth has become more deliberate and thorough, and hasty work has disappeared. In children it is common to combine the extraction of grossly carious teeth with the filling of the less carious ones.

General anæsthetic practice has correspondingly altered, with the result that the brief nasal administrations of nitrous oxide have almost disappeared, at least in private practice, to be replaced by more prolonged endotracheal anæsthesia. This has presented no difficulties for in-patients, but for out-patients, in whom short recovery times are desirable, there has been a problem in administering a non-inflammable anæsthetic agent (now considered essential for dental work), while still retaining the rapid return to consciousness. Different anæsthetists use alternative methods to attain these ends. The method about to be described—namely, the use of nitrous oxide and halothane administered by the endotracheal route—has proved satisfactory in a trial for out-patient dental work.

Method.

The patient is questioned, and examined physically to ascertain that he is in good health and does not present any condition likely to lead to anæsthetic difficulties.

Three drops of "Neo-Synephrin" (1%) are instilled into each nostril to shrink the nasal mucous membrane. For cooperative children and adults, thiopentone to which atropine has been added is injected intravenously, followed by a relaxing agent: gallamine is used for longer procedures, and suxamethonium for shorter ones. The doses of thiopentone and relaxing agent are kept to a minimum consistent with atraumatic intubation. The dental chair is suitably positioned, and after the patient's lungs have been inflated with oxygen, a naso-tracheal tube is introduced and a naso-pharyngeal pack inserted. Respiration is now effected by compressing the rebreathing bag, nitrous oxide is added to the mixture, and the operation commences. As soon as spontaneous respiration reasserts itself to a sufficient degree, halothane is added in the least concentration needed to maintain light anæsthesia. It may be mentioned that although teeth are exquisitely sensitive in the conscious patient, light anæsthesia suffices for dental work.

At the conclusion of the procedure, pure oxygen is administered for two minutes, the pack is removed, the throat cleared by suction and the tube removed. The patient is then placed on the recovery bed in the lateral position.

For small or non-cooperative children, unconsciousness is secured by the administration of ethyl chloride. Then atropine, relaxing agents or thiopentone may be injected intravenously. The procedure as for adults is then followed.

The recovery period is usually short and without vomiting. In this it follows the pattern usually observed in recovery from nitrous oxide and halothane anæsthesia.

Summary.

The greater length of dental procedures performed under general anæsthesia has been noted, and the endotracheal administration of nitrous oxide and halothane, non-inflammable anæsthetic agents, has been suggested as satisfactory for out-patient dental work with a rapid, pleasant recovery.

Addendum.

Since this paper was submitted for publication, the following article, which deals with somewhat different aspects of the subject, has been published:

GOLDMAN, V. (1959), "Fluothane in the Dental Surgery", *Curr. Res. Anesth.*, 38: 192.

Reports of Cases.

PROGRESSIVE CHLORPROMAZINE JAUNDICE DURING PREGNANCY.

By ERIC V. MACKAY.
From the Department of Obstetrics and Gynæcology, University of Melbourne.

TOXIC EFFECTS of chlorpromazine include depression of white blood cell precursors and jaundice due to hepatitis. Jaundice occurs in about 0·5% to 1% of patients receiving chlorpromazine (Shay and Siplet, 1957; Kirsner *et alii*, 1959) and shows obstructive features; the serum levels of bilirubin and alkaline phosphatase are raised, and the result of the flocculation test is negative. The jaundice is usually mild in degree, and of short duration (one to three weeks). However, a number of cases have been described in which the hepatitis, presumably due to chlorpromazine, has lasted for over six months (Azima and Ogle, 1954; Myers *et alii*, 1957; Hoffbauer, 1959), and a number of deaths have occurred (Boardman, 1954; Hollister 1957; Rodin and Robinson, 1958).

In the present case, the onset of jaundice dated from chlorpromazine therapy administered for hyperemesis gravidarum in the first trimester of pregnancy. A progressive deterioration in the patient's condition required interruption of the pregnancy at the twenty-third week. The hepatitis persisted for over twelve months, and the patient developed the features of obstructive biliary cirrhosis with hyperlipidæmia and xanthelasmata.

Clinical Record.

Mrs. A., aged 38 years, was referred to the Clinical Research Unit of the Royal Melbourne Hospital in May, 1957, with jaundice following the administration of chlorpromazine for hyperemesis gravidarum 10 weeks previously. Seven years before she had suffered from mild infectious hepatitis. Two pregnancies previous to this had also been complicated by hyperemesis gravidarum. Seven weeks after her last normal menstrual period, which was on December 27, 1956, the patient experienced severe nausea and vomiting, for which chlorpromazine, in a dosage of 75 mg. per day, was prescribed. Two weeks later she developed persisting jaundice with pale stools, severe pruritus and subsequent bruising, hæmaturia and hæmatemesis.

Examination of the patient on her admission to hospital revealed widespread bruising and scratch marks on her skin; the liver and spleen were not palpable. The uterus corresponded in size to an 18 weeks' pregnancy. Biochemical investigations gave the following results. The serum bilirubin content was 3·2 mg. per 100 ml.; the result of the cephalin flocculation test was negative; the serum alkaline phosphatase content was 60 King-Armstrong units; the hæmoglobin value was 9·7 grammes per 100 ml.; the prothrombin index was 7% of normal. The serum protein, blood urea and serum electrolyte levels were within normal limits. Other biochemical findings are presented in Table I.

After her admission to hospital, the patient complained of severe headache and dizziness. The cerebro-spinal fluid was xanthochromic and had a protein content of 90 mg. per 100 ml., suggesting that an intracranial hæmorrhage had occurred. After the lumbar puncture she noticed severe persisting pain in the groins, hips and thighs.

TABLE I.
Results of Laboratory Investigations.

Investigations.	2.5.57.	13.5.57.	20.5.57.	14.6.57.	8.7.57.	12.8.57.	9.9.57.	10.12.57.	26.2.58.	1.5.58.	10.12.58.
Serum bilirubin content (milligrammes per 100 ml.)	6·4	10·0	—	—	11·7	12·4	3·6	6·0	6·0	3·0	Normal
Cephalin flocculation (24 hours)	Nil	Nil	Nil	Nil	+	+++	Nil	+++	Nil	Nil	Nil
Serum albumin content (grammes per 100 ml.)	3·0	3·3	—	—	2·9	3·6	4·3	3·5	4·4	4·3	4·6
Serum globulin content (grammes per 100 ml.)	3·4	2·9	—	—	3·6	4·0	3·6	4·2	3·5	2·6	2·7
Serum globulin content (grammes per 100 ml.)	0·8	1·0	—	—	1·1	1·4	1·3	2·0	2·5	1·1	1·0
Prothrombin index (percentage of normal)	7	40	100	64	75	52	30	75	—	75	—
Fasting serum lipid content (milligrammes per 100 ml.)	—	—	—	—	4699	1695	4014	2559	—	920	770
Serum cholesterol content (milligrammes per 100 ml.)	—	350	—	504	800	706	800	700	—	460	290
Bromsulphthalein retention, 45 minutes (percentage of administered dose)	—	—	—	—	53·5	—	—	—	—	—	—
Serum alkaline phosphatase content (King-Armstrong units)	60	64	—	74	86	78	92	52	58	52	32
Plasma glutamic oxalacetic transaminase content (units)	—	—	—	71	—	—	136	61	—	38·5	25
Hæmoglobin value (grammes per 100 ml.)	13·1	12·5	—	15·4	13·1	12·1	11·6	9·7	14·8	—	—
Blood sedimentation rate, Westergren (millimetres per hour)	—	23	92	—	—	9	111	—	—	42	62

Flaccid paralysis of both legs and urinary retention developed, and there followed a severe infection of the urinary tract with *Proteus vulgaris*. She became more deeply jaundiced, irrational, disorientated and lethargic.

At the twenty-third week of pregnancy, the patient was transferred to the Royal Women's Hospital, and the pregnancy was terminated soon after by abdominal hysterotomy. It was considered that early liver failure was present. An operative liver biopsy showed the characteristic changes of chlorpromazine jaundice (Figure I).[1] After the operation there was some clinical improvement, but she remained very ill.

By July, 1957, cutaneous xanthelasmata had appeared, and she presented all the features of prolonged obstructive jaundice, with elevated serum levels of alkaline phosphatase, total lipids and cholesterol (Figure II).

By August, 1957, she was gravely ill. Her mental state had deteriorated, with loss of memory, delusions and hallucinations. She was very wasted and jaundice was intense. The persistence of hepatitis prompted the use of cortisone (200 mg. per day). This resulted in a dramatic improvement, and she gained 30 lb. in weight in six weeks. Her mental condition also improved, aided by a course of electroconvulsive therapy.

By February, 1958, she was mentally clear; but jaundice was still present, and the liver was firm, smooth, tender and palpable 2 in. below the right costal margin. The spleen was just palpable. The leg muscles were wasted and weak with absent deep reflexes, and there was patchy anæsthesia over the lower part of the left leg. Improvement continued, and by December, 1958, jaundice had disappeared and the liver was no longer enlarged; xanthelasmata were still present in the eyelids, she could walk freely, and there remained only minor sensory loss.

Biochemical Alterations.

The results of laboratory investigations are detailed in Table I and Figure II. The main features in the early part of the illness were an elevation of the serum levels of bilirubin, alkaline phosphatase and glutamic oxalacetic transaminase, with a depression of the prothrombin index. After termination of the pregnancy there was no improvement in the biochemical findings. The result of the cephalin flocculation test, which was initially negative, became positive about four weeks after the operation, and remained intermittently so for five months. This coincided with the period of marked elevation of serum lipid levels. The administration of cortisone for eight weeks in August, 1957, led to a drop in serum bilirubin level and a return to normal of the result of the cephalin flocculation test. A gradual return to normality of the other biochemical findings followed completion of the course.

[1] For Figure I see art-paper supplement.

Discussion.

Although it is difficult to diagnose chlorpromazine hepatitis with certainty, there is very strong evidence for such a diagnosis in this case. Obstructive jaundice followed a two weeks' course of chlorpromazine therapy, and the clinical, biochemical and histological changes were all characteristic.

There appears to be some disturbance of liver function in a considerable proportion of patients treated with chlorpromazine. Waitzkin (1958) studied 50 patients in whom tests revealed normal liver function prior to the administration of chlorpromazine; after four weeks, only 19 patients had completely normal liver function. Of the other 31 patients, none were jaundiced, but all showed abnormal retention of bromsulphthalein, and 16 in addition had raised serum levels of alkaline phosphatase and transaminase. Dickes *et alii* (1957) reported abnormalities in liver function in 21 of 50 patients during the first month of chlorpromazine therapy, and one patient became jaundiced. Moreover, histological changes in the liver were demonstrable in four of the 18 patients studied by Sims *et alii* (1955), and in five of 16 in another series (Bartholomew *et alii*, 1958), even in the absence of jaundice. As in the present case, hepatitis may result from quite low dosage of the drug, or even from a single dose. There is some evidence that the chlorinated compound is more apt to involve the liver than the related drug promazine (Shay and Siplet, 1958).

Moyer *et alii* (1954) consider that patients with antecedent liver disease are not more susceptible to the toxic effects of chlorpromazine than normal subjects. This is not supported by Bartholomew's series (1958), in which an increase in preexisting abnormality occurred in eight out of nine patients. In the present case, it was thought that the previous history of infectious hepatitis was not relevant to the present illness, in view of the liver biopsy findings.

Chlorpromazine is one of a group of drugs which cause an obstructive type of jaundice in humans, the others including neoarsphenamine, methyl testosterone, thiouracil, sulphonamide and phenylbutazone (Kunkel, 1956). The

essential lesion is an inflammatory reaction, which may be minimal, around the interlobular bile ducts, and bile plugging in interlobular canaliculi. Popper and Schaffner (1959) classify this process as intrahepatic cholestasis. A transition to chronic biliary cirrhosis with xanthomatosis is rare, but has been reported in arsphenamine jaundice (Stolzer *et alii*, 1950) and a well-documented transition from chlorpromazine hepatitis was reported by Myers *et alii* (1957). The present case represents another example.

Continuing liver damage in this patient was indicated by the raised serum levels of alkaline phosphatase and transaminase, which showed roughly parallel rises; maximum values for each were observed five months after the start of the illness, and both levels remained high after 15 months. The transition to the chronic stage was further denoted by high plasma levels of lipids, the rise in which is usually mild and transitory in chlorpromazine hepatitis. Marked elevations are found only in the severest cases, and persistence of hyperlipidæmia may be the sole evidence of activity (Gambescia, 1956). The maximum level of total lipids of 4700 mg. per 100 ml. occurred four months after the onset of jaundice, and xanthelasmata appeared after a further nine months.

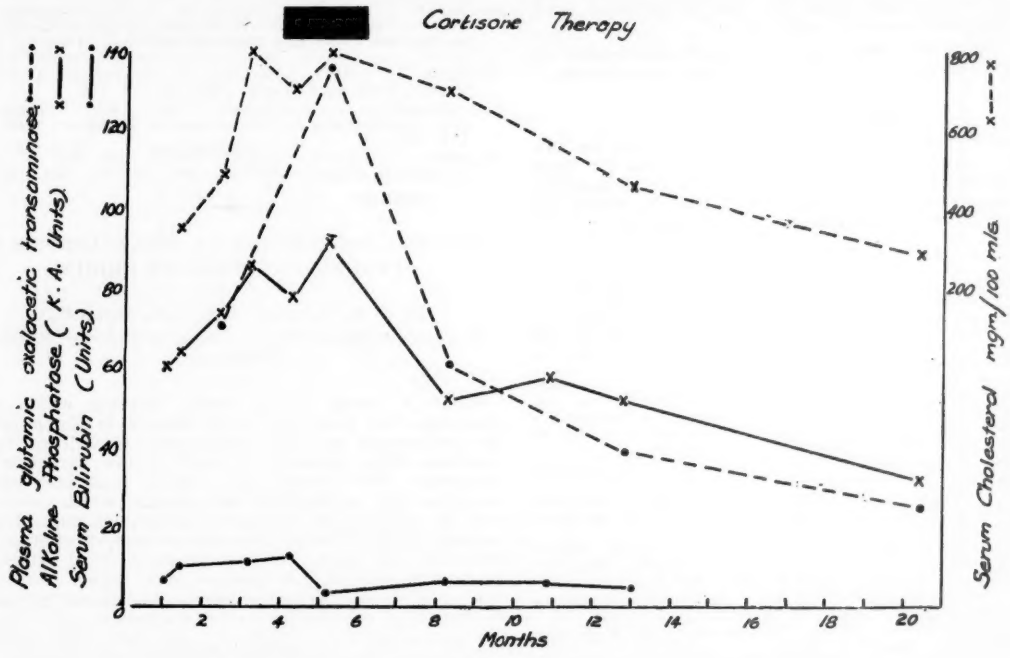

FIGURE II.
Biochemical values during the course of the patient's illness.

It is difficult to assess all the factors responsible for the deterioration in this patient. The early neurological changes were thought to be due to hypoprothrombinæmia, manifestations of which were ecchymoses and intracerebral bleeding; the paraplegia may have had a similar pathogenesis. The spinal lesion with the subsequent cystitis and the termination of pregnancy may have contributed to the continuance of liver-cell damage, for surgical procedures have been known to induce or worsen liver injury in chlorpromazine jaundice (Popper and Schaffner, 1957). Some clinical improvement followed the hysterotomy, but this was not reflected in the results of biochemical tests.

Cortisone has been used in the treatment of severe chlorpromazine jaundice, but reports of its effectiveness have not been consistent. Thus, in the cases reported by Myers *et alii* (1957) and by Hollister (1957) there was little improvement; however, Stein and Wright (1956) noted a rapid fall in serum bilirubin level, loss of jaundice and an increased sense of well-being in their patient, and Gambescia *et alii* (1956) found benefit from a course lasting 30 days. In the present case, there was pronounced clinical improvement after cortisone therapy was begun in the fourth month of the illness, when there seemed little chance of survival. The serum level of bilirubin fell sharply, but the plasma levels of lipids, alkaline phosphatase and glutamic oxalacetic transaminase showed only a slow improvement after the finish of the eight-week course of cortisone.

The role of chlorpromazine in the treatment of hyperemesis gravidarum requires careful appraisal. About 60% of pregnant women experience vomiting at some period (Fitzgerald, 1955), but few require admission to hospital. In the year 1953, at the Royal Women's Hospital, Melbourne, less than 0·5% of 5850 elective admissions were for hyperemesis gravidarum. Moreover, the majority of such patients admitted to hospital are relieved without specific measures (Fitzgerald, 1956).

Chlorpromazine has been employed in hyperemesis gravidarum because of its known antiemetic properties. Early reports (Moyer *et alii*, 1955; Coopersmith, 1956) were very favourable, in that significant improvement occurred in over 80% of cases within one or two days, and no cases of jaundice occurred. Hall (1956) reported 42 pregnant patients with hyperemesis who received chlorpromazine; 30 were cured and five improved. Jaundice was observed in 10% of these patients. It occurred only in patients whose treatment was commenced in the outpatient department, and who failed to respond to the drug and continued to vomit during its administration.

Minor disturbances in the results of liver function tests are frequently found in pregnancy (Thorling, 1955), and may indicate hepatic strain due to increased metabolic demands; considerable aggravation must occur if severe hyperemesis supervenes. Hall (1956) suggested that in pregnancy the liver might be more susceptible to

chlorpromazine toxicity, and this was so in the present case and in the cases reported by Gebhart *et alii* (1958) and by Hoffbauer (1959). It is submitted that therapy with these compounds, at least for nausea and vomiting of pregnancy, should be given only after careful consideration and when other therapy has been ineffective. Such occasions should be few in number.

Summary.

Severe prolonged jaundice occurred in a patient given chlorpormazine for hyperemesis gravidarum.

The pregnancy was terminated at the twenty-third week, owing to deterioration in the patient's condition and incipient liver failure. The liver disease progressed, and showed the features of prolonged obstructive jaundice with xanthelasmata and hyperlipidæmia. Pronounced improvement coincided with the use of cortisone, and almost complete recovery occurred.

It is considered that the use of chlorpromazine is inadvisable in most cases of hyperemesis gravidarum.

Acknowledgements.

I wish to thank Professor S. L. Townsend and Dr. Ian Wood for permission to publish this case and for their helpful advice, Dr. I. R. Mackay for advice in preparation of the paper, and Dr. S. Wieden and Miss M. Smith for their help with the biochemical investigations.

References.

AZIMA, H., and OGLE, W. (1954), "The Effect of Largactil in Mental Syndromes", *Canad. med. Ass. J.*, 71: 116.

BARTHOLOMEW, L. G., CAIN, J. C., FRAZIER, S. H., PETERSEN, M. C., FOULK, W. T., SOULE, E. H., FLEISCHER, G. A., and OWEN, C. A. (1958), "Effect of Chlorpromazine on the Liver", *Gastroenterology*, 34: 1096.

BENARON, H. B. W., DORR, E. M., RODDICK, W. J., JOHNSON, R. P., GOSSACK, L., and TUCKER, B. E. (1955), "The Use of Chlorpromazine in the Obstetric Patient. A Preliminary Report. I. In the Treatment of Nausea and Vomiting of Pregnancy", *Amer. J. Obstet. Gynec.*, 69: 776.

BOARDMAN, R. H. (1954), "Fatal Case of Toxic Hepatitis Implicating Chlorpromazine", *Brit. med. J.*, 2: 579.

COOPERSMITH, G. E. (1956), "Thorazine-Dexedrine Combination in Treatment of Nausea and Vomiting of Pregnancy", *Obstet. and Gynec.*, 8: 235.

DICKES, R., SCHENKER, V., and DEUTSCH, L. (1957), "Serial Liver-Function and Blood Studies in Patients Receiving Chlorpromazine", *New Engl. J. Med.*, 256: 1.

FITZGERALD, J. P. B. (1955), "The Effect of Promazine in Nausea and Vomiting of Pregnancy", *N.Z. med. J.*, 54: 215.

FITZGERALD, J. P. B. (1956), "Epidemiology of Hyperemis Gravidarum", *Lancet*, 1: 660.

GAMBESCIA, J. M., IMBRIGLIA, J., GALAMAGA, P., and WINKELMAN, W. (1956), "Jaundice Associated with the Administration of Chlorpromazine", *Gastroenterology*, 30: 735.

GEBHART, W. F., VAN OMMEN, R. A., MCCORMACK, L. J., and BROWN, C. H. (1958), "Chlorpromazine Jaundice: Clinical Course, Hepatic Function Tests and Pathologic Findings—Summary of 20 Cases", *A.M.A. Arch. intern. Med.*, 101: 1085.

GRAHAM, G. S. (1957), "Chlorpromazine Jaundice in a General Hospital", *Brit. med. J.*, 2: 1080.

HALL, R. E. (1956), "The Treatment of Hyperemesis Gravidarum with Chlorpromazine", *Amer. J. Obstet. Gynec.*, 71: 285.

HOFFBAUER, F. W. (1959), "Clinical Aspects of Jaundice Resulting from Intrahepatic Obstruction", *J. Amer. med. Ass.*, 169: 1453.

HOLLISTER, L. E. (1957), "Allergy to Chlorpromazine Manifested by Jaundice", *Amer. J. Med.*, 23: 870.

KIRSNER, J. B., DOOLEY, J. E., SCOTT, G. E., and KRAFT, S. C. (1959), "Gastroenterology", *Ann. Rev. Med.*, 10: 21.

KUNKEL, H. G. (1956), "Diseases of the Liver", edited by L. Schiff, Lippincott, Philadelphia: 477.

MOYER, J. H., KENT, B., KNIGHT, R., MORRIS, G., HIGGINS, R., and HANDLEY, C. A. (1954), "Laboratory and Clinical Observations on Chlorpromazine: Hæmodynamic and Toxicological Studies", *Amer. J. med. Sci.*, 227: 283.

MOYER, J. H., KINROSS-WRIGHT, V., and FINNEY, R. M. (1955), "Chlorpromazine as Therapeutic Agent in Clinical Medicine", *A.M.A. Arch. intern. Med.*, 95: 202.

MYERS, J. D., OLSEN, R. E., LEWIS, J. H., and MORAN, T. J. (1957), "Xanthomatous Biliary Cirrhosis following Chlorpromazine, with Observations Indicating Overproduction of Cholesterol, Hyperprothrombinæmia and the Development of Portal Hypertension", *Trans. Ass. Amer. Phycns.*, 70: 243.

POPPER, H., and SCHAFFNER, F. (1951), "Pathology of Jaundice Resulting from Intrahepatic Cholestasis", *J. Amer. med. Ass.*, 169: 1453.

POPPER, H., and SCHAFFNER, F. (1957), "Liver: Structure and Function", McGraw-Hill, New York: 404.

RODIN, A. E., and ROBINSON, D. M. (1958), "Fatal Toxic Hepatitis Following Chlorpromazine Therapy", *A.M.A. Arch. Path.* 66: 170.

SHAY, H., and SIPLET, H. (1957), "Study of Chlorpromazine Jaundice, Its Mechanism and Prevention", *Gastroenterology*, 32: 571.

SHAY, H., and SIPLET, H. (1958), "Relationship of Chemical Structure of Chlorpromazine to its Liver Sensitizing Action", *Gastroenterology*, 35: 16.

SIMS, J. L., BREMER, E. M., and HUSTON, E. S. (1955), "Chlorpromazine: Changes in Hepatic Histology in the Absence of Jaundice", *J. Lab. clin. Med.*, 46: 952.

STEIN, A. A., and WRIGHT, A. W. (1956), "Hepatic Pathology in Jaundice due to Chlorpromazine", *J. Amer. med. Ass.*, 161: 508.

STOLZER, B. L., MILLER, G., WHITE, W. A., and ZUCKERBROD, M. (1950), "Postarsenical Obstructive Jaundice Complicated by Xanthomatosis and Diabetes Mellitus", *Amer. J. Med.*, 9: 124.

THORLING, L. (1955), "Jaundice in Pregnancy. A Clinical Study", *Acta. med. scand.*, Supp. to Vol. 151.

VAN OMMEN, R. A., and BROWN, C. H. (1955), "Obstructive-type Jaundice due to Chlorpromazine", *J. Amer. med. Ass.*, 157: 321.

WAITZKIN, L. (1958), "Hepatic Dysfunction due to Chlorpromazine Hypersensitivity", *Ann. intern. Med.*, 49: 607.

SCALENE NODE BIOPSY IN THE DIAGNOSIS OF PYREXIA OF UNKNOWN ORIGIN.

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WHEN a young person suffers pyrexia which defies diagnosis, this occasions much concern to the physician, the pathologist and the radiologist, as well as to the relatives, who clamour to be told the diagnosis and prognosis. The present case report illustrates such a problem, and emphasizes the success which ultimately will be achieved by continuous meticulous clinical observations, X-ray examinations and laboratory studies. The diagnosis was finally revealed by radiological evidence of increasing size of the mediastinum, which led to the taking of a scalene node biopsy. The dramatic response to treatment contributed to the diagnosis.

Clinical Record.

A girl, aged 15 years, was first examined in September, 1958, when she complained of five months' anorexia, malaise, feverishness, constipation and non-productive cough, with the loss of one stone in weight. She was pale and thin and appeared ill; the pulse rate was 120 per minute. During the following eight weeks she had a high intermittent fever and lost six pounds in weight. The positive laboratory findings were the presence of hypochromic microcytic anæmia with an active bone marrow indicating iron deficiency. The fæces gave persistently positive results to tests for occult blood. The erythrocyte sedimentation rate was elevated to 106 mm. in one hour. Negative results were obtained from agglutination tests for *Salmonella typhi, S. paratyphi* A and B and *Brucella abortus*, from the Paul-Bunnell test and from the Wassermann test. Culture of the fæces, blood and urine produced no growth of pathogens, and the results of a Casoni skin test, a liver biopsy and culture, microscopic examination of the urine, the L.E. cell test and serum glutamic oxalacetic transaminase estimation were all normal.

In view of the deterioration in the patient's condition, a course of penicillin (1,000,000 units every six hours) was given for one week, and this was followed by a course of streptomycin (1 gramme every alternate day), with isoniazid (50 mg. three times daily) for two weeks. Neither of these empirical courses produced any effect, nor did a course of emetine hydrochloride (30 mg. by intramuscular injection twice a day for three days).

Six weeks after her admission to hospital, during the seventh month of the illness, an X-ray of the chest revealed widening of the upper mediastinal shadow (Figures I and II).[1] Electrophoresis showed a lowered serum albumin level of 3·5 grammes per 100 ml., associated with a raised alpha-2 globulin level of 1·2 grammes per 100 ml. The serum hexosamine level was elevated to 200 mg. per 100 ml. (normal, 80 to 120 mg. per 100 ml.). A lymph node was removed from the right groin under general anæsthesia, but the histological findings were normal, and there was no growth on culture. One week later, on the recommendation of the thoracic surgeon, the right scalene node was excised under local anæsthesia. This was found deep to the deep cervical fascia in the fat in front of the scalenus anterior. Microscopic examination of sections revealed general increase of hyaline reticulum, with diffuse arrangement of lymphocytes in the medulla, giant cells with irregular or multiple nuclei which stained darkly and fairly numerous eosinophils. The changes were diagnostic of Hodgkin's disease (Figure III).

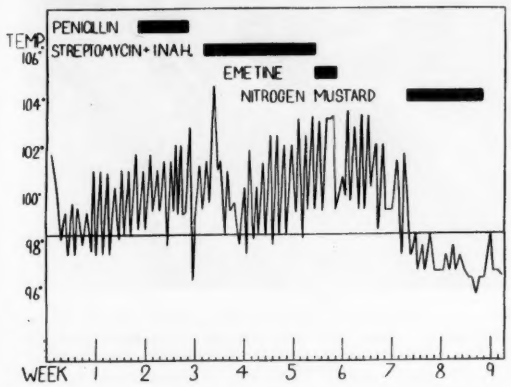

FIGURE IV.

The dramatic effect of nitrogen mustard on the sustained pyrexia contrasts strikingly with the lack of response to empirical treatment, in this case of Hodgkin's disease proved by scalene node biopsy. Nitrogen mustard was given in the ninth month of the illness, and three months later the patient appeared to be in good health.

Treatment with nitrogen mustard by intravenous injection produced an immediate and sustained response, a dramatic contrast to the lack of response to antibiotics (Figure IV). The temperature fell to normal after the first dose, and the patient improved remarkably in appearance and sense of well-being, gaining two pounds in weight in the first week. When she was last examined three months later, she was in good health.

Comment.

This case demonstrates the value of making serial X-ray examinations to reveal the appearance of mediastinal enlargement in prolonged undiagnosed pyrexia. It emphasizes also the superiority at that stage of a scalene node biopsy, because of the close anatomical relationship of the scalene node to the mediastinum, compared with biopsy of nodes from other more accessible regions which most probably will not be involved. In skilled and experienced hands scalene node biopsy can be performed under local anæsthesia without distress to the patient (Shields *et alii*, 1958).

The lowered serum albumin level occurs frequently in patients with malignant disease, probably owing to nutritional impairment (Arends *et alii*, 1954). The raised serum alpha-2 globulin level has been ascribed by these authors to the systemic reaction due to fever and tissue necrosis. After treatment, the serum albumin level rose to 3·6 grammes per 100 ml. and the serum alpha-2 globulin level fell to 0·8 gramme per 100 ml. The reversion to normal following successful treatment of Hodgkin's disease also has been observed by others (Wall, 1958). Moreover, the serum hexosamine level fell from 200 to 124 mg. per 100 ml. (the normal level).

Weiden (1958) had previously found high serum levels of hexosamine in patients with Hodgkin's disease and recommended this test as a valuable aid in the differentiation of Hodgkin's disease from chronic infections, in which there was a less pronounced rise (see page 207 of this issue). The high level was considered to be a non-specific index of tissue destruction and proliferation.

[1] For Figures I, II and III see art-paper supplement.

Acknowledgements.

I wish to express my thanks to Dr. C. H. Fitts for permission to publish this case, to Mr. J. I. Hayward who performed the scalene node biopsy, and to Dr. J. D. Hicks for the histological findings. The photographs were prepared by Mr. R. Inglis, Clinical Photographer at the Royal Melbourne Hospital.

References.

ARENDS, T., COONRAD, E. V., and RUNDLES, R. W. (1954), "Serum Proteins in Hodgkin's Disease and Malignant Lymphoma", *Amer. J. Med.*, 16: 833.

SHIELDS, T. W., LEES, W. M., and FOX, R. T. (1958), "The Diagnostic Value of Biopsy of Non-Palpable Scalene Lymph Nodes in Chest Diseases", *Ann. Surg.*, 148: 184.

WALL, R. L. (1958), "The Use of Serum Protein Electrophoresis in Clinical Medicine", *A.M.A. Arch. intern. Med.*, 102: 618.

WEIDEN, S. (1958), "Serum Hexosamine Levels in Health and Disease", *J. clin. Path.*, 11: 177.

TETRALOGY OF FALLOT WITH ORIGIN OF THE LEFT CORONARY ARTERY FROM THE RIGHT PULMONARY ARTERY.[1]

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OVER fifty cases of origin of the left coronary artery from the pulmonary trunk have been reported. Associated congenital cardiac anomalies appear to be very rare. One of these was described by Alexander and Griffith (1956), which was associated with infantile coarctation of the aorta and patent ductus arteriosus. The case presented here was associated with tetralogy of Fallot.

Clinical Record.

A male child was born on June 13, 1958; his birth weight was 6 lb. 12 oz. The pregnancy had been uneventful, and his mother had not suffered from rubella or other illnesses. He was born after a normal labour, but was noticed to be always slightly cyanosed; the cyanosis increased slightly when he cried. Otherwise he appeared to be quite well and took his feeds satisfactorily. No bruits or other abnormal signs were apparent in the chest. Both testicles were undescended. An X-ray examination of the chest on June 16 revealed a typical silhouette of tetralogy of Fallot, showing the *cœur en sabot*, the cardiac apex lifted away from the diaphragm, widening of the superior mediastinum to the right, and avascular lung fields (Figure I)[2]. This was the diagnosis then made. As no treatment was then indicated and his condition was good, he was discharged from hospital at the age of eight days, being breast-fed and weighing 7 lb. 2 oz.

He remained well, but was always slightly cyanosed, more so when he cried. He took his feeds satisfactorily, without dyspnœa or other symptoms. On July 9, when he was three and a half weeks old, he awoke at 11 a.m., refused a feed and started to cry a great deal. He became more and more cyanosed, and his respirations became rapid.

[1] With a description of the electrocardiographic findings by D. C. Fison, Medical Superintendent, Brisbane Children's Hospital, Brisbane.

[2] For Figures I and II, see art-paper supplement.

On examination of the baby at the Brisbane Children's Hospital, the essential findings were as follows. He was very cyanosed, with rapid respirations. The temperature in the axilla was 99·4° F. The limbs were pulseless, and the pulse rate on auscultation was 110 per minute. The venous pressure did not seem to be raised. The apex beat could not be palpated. On auscultation, soft presystolic and systolic bruits were heard, with triple rhythm. The breath sounds were diminshed in the right side of the chest, with occasional rhonchi. A provisional diagnosis of congenital cardiac malformation, cardiac failure and pneumonia was made. He was treated with oxygen, tetracycline given intramuscularly and digoxin given intramuscularly. X-ray films of the chest were taken and showed a dramatic change from the previous ones (Figure II). The cardiac shadow was grossly enlarged, especially to the right and anteriorly. The apex was still lifted off the diaphragm, and the lung fields still appeared to be avascular. These findings were thought to be consistent with tricuspid atresia with atrial septal defect, or Ebstein's malformation. The last-mentioned is when part of the attachment of the leaflets of the tricuspid valve is at a lower level than normally, so that part of the right ventricular cavity is anatomically continuous with the right atrial cavity. An electrocardiogram was taken (see below). Treatment was of no avail, and he died 11 hours after the commencement of the attack.

Autopsy Findings.

The essential findings were as follows. The body was that of a well-nourished white male baby weighting 8 lb. 3·5 oz. Clubbing of fingers and toes was not present. There was general vascular engorgement of the body. Both testicles were undescended and were just internal to the internal inguinal rings. Both lungs showed patches of consolidation resembling early bronchopneumonia.

The heart was moderately enlarged. It was 6·2 cm. long, 5 cm. across the waist, and 3·7 cm. in the sagittal direction. The right atrium was fairly enlarged, about 2·7 cm. in diameter. Its relations with both venæ cavæ and the coronary sinus were normal. The interatrial septum was normal, and the foramen ovale was about half closed, with normal valve action. The right ventricle was moderately dilated with a hypertrophied wall 3 or 4 mm. thick. The tricuspid and mitral valves were normal, and there was no evidence of Ebstein's malformation. The left atrium was about normal in size, and was entered by four normal pulmonary veins. The left ventricle was moderately dilated, mainly owing to an aneurysmal type of bulging of its wall. On the external surface of the left ventricle in the bulging area there were numerous fine thin-walled blood vessels, too fine to be dissected out. The posterior aspect of the left ventricle near the interventricular septum was about 4 mm. thick, but the remainder was narrowed, down to a thickness of about 2 mm. in the centre of the affected area. On examination of sections, the myocardium there showed yellow patches resembling infarction. The interventricular septum anteriorly also showed these changes. There was a defect about 7 mm. in diameter in the upper part of the interventricular septum, with overriding of the aorta. The pulmonary conus was slightly narrowed. The pulmonary valve at the cusps was very stenosed, only about 1·5 mm. diameter. The pulmonary trunk was narrow, about 9 mm. in circumference, and its branches were of similar proportions. The ductus arteriosus was almost closed, a lumen about 3 mm. in circumference remaining. The aorta was about normal in size. The right coronary artery (Figure III), arose normally and had a normal course and distribution as far as careful dissection could tell, except that its interventricular branch passed only about two-thirds of the way up the inferior interventricular groove, a common variation. The main anastomoses with the left coronary artery and its branches were too fine to be dissected out. The left coronary artery arose inferiorly from the right pulmonary artery, just after the origin of the latter (Figure III). It was of about normal calibre. It passed inferiorly behind the pulmonary trunk, curving around it to the left, to enter the atrio-ventricular groove just to the left of the pulmonary trunk, where it gave off a large interventricular branch. This branch ramified over its usual distribution as well as the apical region, extending to about one-third of the way along the inferior interventricular groove. The remainder of the left coronary artery appeared to ramify over its normal distribution.

Microscopic Examination.

The lungs showed evidence of venous congestion and early bronchopneumonia.

In the heart, sections taken from the anterior wall of the left ventricle, the anterior end of the interventricular septum and the papillary muscles of the left ventricle showed the features typical of origin of the left coronary artery from the pulmonary trunk in the absence of

FIGURE III.

The heart. The points of the two prominent pins are in the origins of the coronary arteries; 1, aorta; 2, pulmonary trunk.

other cardiac anomalies. There were patches of necrosed muscle, frequently calcified, with much fibrosis apparently in the process of replacing that necrosed muscle. Muscle fibres adjacent to these areas showed degenerative features. No inflammatory exudate was apparent. Slight endocardial fibrosis may have been present. There were numerous blood spaces in the affected myocardium, but not in non-affected regions. These were similar to the "myocardial sinuses" discussed by Kaunitz (1947). They communicated freely with many vessels resembling dilated thin-walled veins in the pericardium. These were the thin-walled vessels seen on the surface macroscopically. In numerous sections taken, there was no definite evidence as to whether these sinuses communicated with the left ventricle or the coronary arteries; but some of them extended into the endocardium, suggesting the former communication. The dilatation of the veins in the pericardium suggests that the sinuses transported large volumes of blood. Injection studies were not performed on this subject. The injection mixture recommended by Schlesinger (1957) should prove of great value in the study of these cases, especially in relation to the coronary circulation and the myocardial sinuses. This mixture is radio-opaque, and remains fixed in the vessels after ordinary fixation procedures, where it can be again studied microscopically after ordinary histological procedures have been undertaken. The fibrous and other lesions appeared to be oldest in the central regions of the affected myocardium, with more recent extension peripherally. The posterior parts of the left ventricle and interventricular septum, and the right ventricle, showed only myocardial hypertrophy. In sections of both coronary arteries and their branches no abnormalities were detected.

Summary of the Autopsy.

The autopsy findings may be summarized as follows: (i) tetralogy of Fallot; (ii) origin of the left coronary

artery from the right pulmonary artery, with typical ischæmic changes in the left ventricular wall; (iii) passive congestion of the systemic and pulmonary circulations; (iv) bronchopneumonia.

The Electrocardiographic Findings.

The following discussion of the electrocardiographic findings has been contributed by Dr. F. C. Fison.

The electrocardiogram taken on July 9 (Figures IV to X) showed the following characteristics. The rate was 120 beats per minute, and regular sinus rhythm was present. P waves measured 0·08 second in duration and

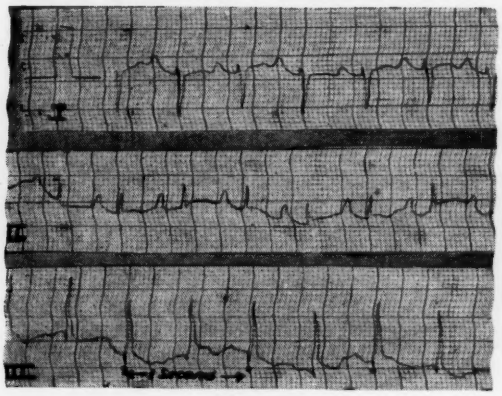

FIGURE IV.

were of high voltage, being approximately 2·3 mm. in height in lead II and rather typical *P* pulmonale, indicative of right atrial hypertrophy. The *P–R* interval measured 0·19 second. As the upper limit of normal for age and rate is given by Ashman and Hull (1941) as 0·135 second, this represents a moderate first-degree auriculo-ventricular block. The Q–T duration measured

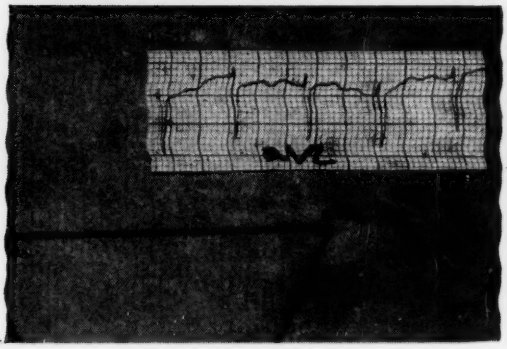

FIGURE V.

0·29 second, which by Ashman and Hull's standards is a value just slightly above the mean normal for age and rate of this patient. The ventricular pattern showed a moderate degree of right axis deviation, the mean electric axis of the QRS complex when plotted on Einthoven's triangle being +127°. However, it must be remembered that the subject was but one month old, and in infancy this axis may be even +130° and still be within normal limits. Ventricular complexes further showed marked clockwise rotation of the heart on its longitudinal axis. This was evidenced by the *QR* pattern in aVR and the right ventricular (*RS*) complexes, with deep *S* waves in precordial leads extending as far to the left as V_6. The period of onset of intrinsicoid deflection (ventricular activation time) was 0·035 second in lead V_1, which is well above the average given by Ziegler of 0·020 second, and even above Ziegler's maximum for this age (0·030 second). Similarly, the ventricular activation time in V_2 measured 0·035 second, against a normal average of 0·017 and maximum of 0·022 second (Ziegler, 1951). The ventricular activation times in V_4, V_5 and V_6 were within normal limits. The *R* wave in V_1 was 10 mm. in height and this by adult standards is very high. However, again it must be remembered that the subject was but an infant, and the algebraic sum of the *R* and *S* waves in this lead can be seen to be only +5 mm., whereas normal values for month-old babies range from +15 to −2 mm. (Alimurung et alii, 1951). From the clockwise rotation, the increased ventricular activation time over

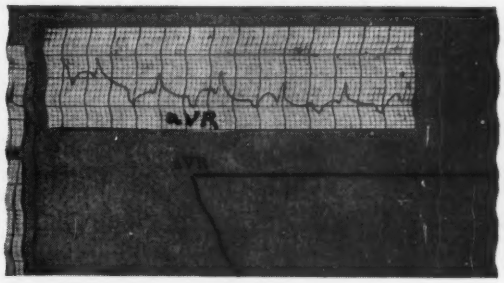

FIGURE VI.

the right half of the precordium and the evidence for right atrial hypertrophy, it was therefore inferred that right ventricular hypertrophy was present, a finding which, with the atrial hypertrophy, was substantiated at autopsy.

Also it will be noted that, although clockwise rotation is so marked that *RS* (right ventricular) complexes extend to V_6, there is no appearance of left ventricular

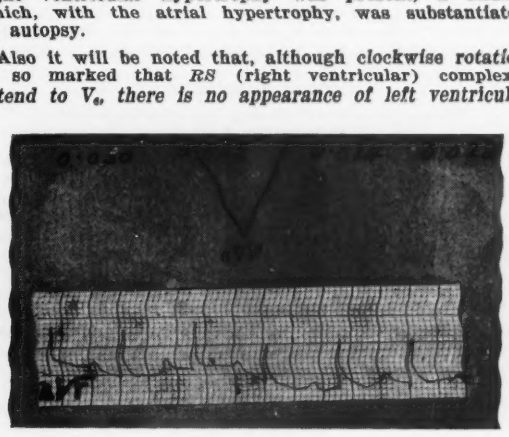

FIGURE VII.

or even back of the heart (*QR*) complexes in V_1 or V_{3R}. In other words, electrodes placed anywhere on the precordium from V_{3R} to V_6 described right ventricular complexes, indicating that this ventricle occupied the entire precordium. As the electrocardiographic evidence for right ventricular hypertrophy was but moderate, the only reasonable deduction was that it was caused by right ventricular dilatation, a description of the heart which was also shown by autopsy to be true.

Such was the electrocardiographic interpretation made during life; but it is interesting now to view the electrocardiogram in retrospect, bearing in mind the anomalous origin of the left coronary artery with the consequent fibrosis of the left half of the myocardium. However, the usual electrocardiographic features of such a malformation were quite absent. One would have

expected to find the usual features of left ventricular ischæmia, in the form of deep inversion of the *T* waves in the standard limb leads and left precordial leads, and possibly also the characteristics of infarction, such as deep *Q* waves in lead I and *QS* complexes in the left chest leads. However, there is a little evidence of left ventricular ischæmia present in the from of low *T* waves in the limb leads and over the left half of the precordium. For example the *T* wave in aVF (which shows typically left ventricular *QR* complexes) is practically isoelectric, and while this is not unknown in normal infants' hearts, the average height of such *T* waves is approximately 2·5 mm. Again, the amplitude of the *T* wave in lead V_6 is but 0·5 mm., whereas the normal for an infant is +1·0 to +4·0 mm. It will, however, be appreciated that these are no more than suggestive of left ventricular ischæmia. It is possible that the first degree auriculo-ventricular block may have been

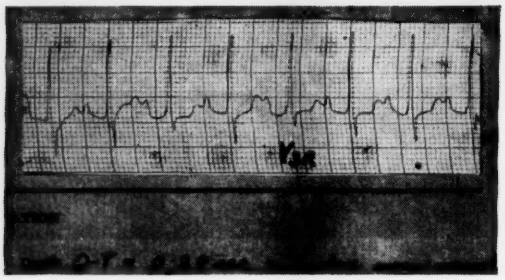

FIGURE VIII.

caused by partial interference with the full blood supply which irrigates the vicinity of the auriculo-ventricular node and the first part of the bundle of His, but it could equally be due to the septal defect which was present.

General Discussion.

Origin of Both Coronary Arteries from the Pulmonary Trunk.

Cases in which both coronary arteries originate from the pulmonary trunk are very rare, and are commonly associated with other cardiac anomalies. The patient's life is usually very short (Tedeschi and Helpern, 1954). A case of especial interest is that of Williams *et alii* (1951), which was associated with tetralogy of Fallot.

Origin of the Right Coronary Artery from the Pulmonary Trunk.

This anomaly appears to be very rare, and has been an incidental finding at autopsy on subjects who have died from unrelated causes (Jordan *et alii*, 1950).

Origin of the Left Coronary Artery from the Pulmonary Trunk.

Subjects in whom the left coronary artery originates from the pulmonary trunk are those who develop infarction and fibrosis of the left ventricular wall. The history and findings are usually typical. The infants are usually well until a few months of age, when they develop paroxysms of screaming and drawing up of the legs, severe sweating, tachypnœa, pallor and sometimes cyanosis. These occur especially after feeds, and may be attacks of angina pectoris. X-ray examination shows enlargement of the heart, particularly the left ventricle. The cardiac pulsations are weak or diminished, and sometimes a cardiac aneurysm may be visualized. Rarely, areas of calcification of the myocardium are seen. The electrocardiogram usually shows an appearance similar to that of anterior infarction. Typical features are inversion of the *T* waves in leads I and II, low *QRS* complexes with deep *Q* waves in the leads over the left ventricle, and commonly left axis deviation (after Bassis and Sheinkopf, 1955, and Kittle *et alii*, 1955). Clinically, severe aortic stenosis may be suspected. The classical thrill and murmur of that condition may not appear until later in childhood. Also, a systolic murmur is often heard along the left border of the sternum with an anomalous left coronary artery. The main differential features are the absence of a grossly enlarged heart and absence of deep *Q* waves across the left side of the precordium in aortic stenosis. Endocardial fibroelastosis may produce a clinical picture identical with anomalous left coronary artery; but the *Q* waves are usually not so prominent, and no *QS* waves are present in endocardial fibroelastosis. The angiocardiogram in anomalous left coronary artery shows a thin, dilated left

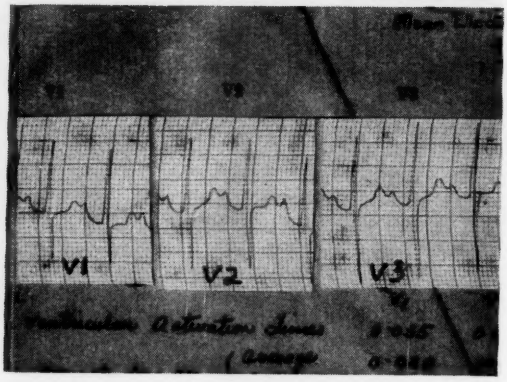

FIGURE IX.

ventricular wall; but in endocardial fibroelastosis the left ventricle shows a thick wall, and this procedure should also differentiate aortic stenosis. Other conditions to be considered are acute glomerulonephritis, coarctation of the aorta and patent ductus arteriosus. Rhabdomyoma and glycogen-storage disease are rare conditions that

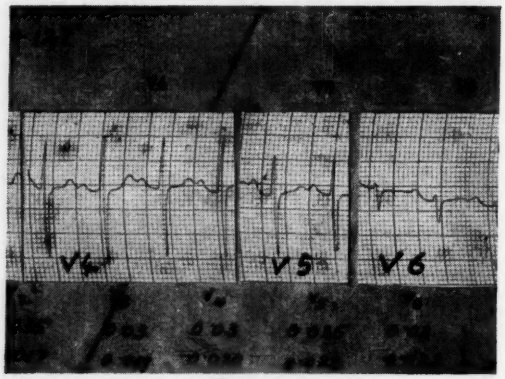

FIGURE X.

may be difficult to differentiate. The anomalous coronary artery can be definitely diagnosed by coronary arteriography (Case *et alii*, 1958). As the life expectancy without surgery is usually only a matter of weeks after symptoms have developed, and as the condition is probably progressive, diagnosis and operation are a matter of urgency.

Dynamics of the Circulation of Anomalous Left Coronary Artery.

It seems that the development of the high aortic pressure while the pulmonary pressure remains low produces dilatation of the anastomoses between the branches of the coronary arteries. The result is that soon the

blood flow in the left coronary artery, presumably initially from the pulmonary trunk, is now from the right coronary artery via the anastomoses into the left coronary artery and thence into the pulmonary trunk. Although the left ventricle is now being perfused by aortic blood, the pressure remains low, in the presence of what is similar to an arterio-venous fistula. For evidence supporting this, see Apley *et alii* (1957), Edwards (1958) and Case *et alii* (1958).

Surgery.

The treatment suggested by Case *et alii* (1958) is ligation of the anomalous artery near the pulmonary trunk, if at operation there is evidence that this will improve the cardiac circulation. If there is no such evidence they suggested the creation of stenosis of the pulmonary trunk; but they thought that the first suggestion might suffice for all cases, but further work was needed. They quoted three cases in which the anomalous artery had been ligated. Other surgical procedures considered include de-epicardialization and pericardial talcum powder *poudrage* (Sabiston, 1958), transplantation or anastomosis of the anomalous vessel (Apley *et alii*, 1957) and excision of the infarcted area (Apley *et alii*, 1957). Paul and Robbins (1958) have had encouraging results in a case in which *poudrage* was the treatment; this is a procedure which they also found encouraging for the treatment of endocardial fibroelastosis.

Summary.

A case is presented of tetralogy of Fallot with origin of the left coronary artery from the right pulmonary artery. The electrocardiogram in this case and the main features of origin of main coronary arteries from the pulmonary trunk are discussed.

Acknowledgement.

I wish to thank Dr. D. C. Fison, Medical Superintendent of the Brisbane Children's Hospital, who kindly discussed the electrocardiogram, for his permission to publish this case.

References.

ALEXANDER, R. W., and GRIFFITH, G. C. (1956), "Anomalies of the Coronary Arteries and their Clinical Significance", *Circulation*, 14: 800.

ALIMURUNG, M. M., JOSEPH, L. G., NADAS, A. S., and MASSELL, B. F. (1951), "Unipolar Precordial and Extremity Electrocardiogram in Normal Infants and Children", *Circulation*, 4: 420.

APLEY, J., HORTON, R. E., and WILSON, M. G. (1957), "The Possible Role of Surgery in the Treatment of Anomalous Left Coronary Artery", *Thorax*, 12: 28.

ASHMAN, R., and HULL, E. (1941), "Essentials of Electrocardiography for the Student and Practitioner of Medicine", Macmillan, New York; cited by Lipman, B. S., and Massie, E., *loco citato*.

BASSIS, M. L., and SHEINKOPF, J. A. (1955), "Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery", *Ann. intern. Med.*, 42: 983.

CASE, R. B., MORROW, A. G., STAINSBY, W., and NESTOR, J. O. (1958), "Anomalous Origin of the Left Coronary Artery: The Physiologic Defect and Suggested Surgical Treatment", *Circulation*, 17: 1062.

EDWARDS, J. E. (1958), "Anomalous Coronary Arteries with Special Reference to Arteriovenous-Like Communications", *Circulation*, 17: 1001.

JORDAN, R. A., DRY, T. J., and EDWARDS, J. E. (1950), "Anomalous Origin of the Right Coronary Artery from the Pulmonary Trunk", *Proc. Mayo Clin.*, 25: 673.

KAUNITZ, P. E. (1947), "Origin of Left Coronary Artery from Pulmonary Artery: Review of the Literature and Report of Two Cases", *Amer. Heart J.*, 33: 182.

KITTLE, C. F., DIEHL, A. M., and HEILBRUNN, A. (1955), "Anomalous Left Coronary Artery Arising from the Pulmonary Artery: Report of a Case and Surgical Consideration", *J. Pediat.*, 47: 198.

LIPMAN, B. S., and MASSIE, E. (1956), "Clinical Unipolar Electrocardiography", Year Book Publishers, Chicago.

PAUL, R. N., and ROBBINS, S. G. (1958), "Surgical Treatment for Endocardial Fibroelastosis or Anomalous Left Coronary Artery: Four Years' Experience with Poudrage", *Amer. J. Cardiol.*, 1: 694.

SABISTON, D. C. (1958), personal communication with Case *et alii*, *loco citato*.

SCHLESINGER, M. J. (1957), "New Radiopaque Mass for Vascular Injection", *Lab. Invest.*, 6: 1.

TEDESCHI, C. G., and HELPERN, M. M. (1954), "Heterotopic Origin of Both Coronary Arteries from Pulmonary Artery; Review of Literature and Report of Case not Complicated by Associated Defects", *Pediatrics*, 14: 53.

WILLIAMS, J. W., JOHNSON, W. S., and BOULWARE, J. R., JR. (1951), "A Case of Tetralogy of Fallot with Both Coronary Arteries Arising from the Pulmonary Artery", *J. Fla. med. Ass.*, 37: 561.

ZIEGLER, R. F. (1951), "Electrocardiographic Studies in Normal Infants and Children", Thomas, Springfield.

A VEIN GRAFT TO THE BRACHIAL ARTERY.

By J. W. GRAHAM,
Sydney.

THE brachial artery has a number of collateral vessels, chief among which is the profunda brachii. Because of this, division of the brachial artery alone is usually without harmful effect. Two patients illustrating this were seen within a few weeks of one another, during 1958. Each had sustained a brachial artery division in a car accident. In each the collateral vessels were intact. Misguidedly, an attempt was made to restore continuity in the first of these cases, with the use of vein graft. Two weeks afterwards the skin wound gaped a little at one point and this revealed the vein graft, blocked by thrombus. Despite this, the patient made a complete recovery and his radial pulse could be felt at the wrist. After this experience, the second case was treated by simple ligature of both ends of the divided artery. The result was a hand with a good circulation.

During the same year, a third case of severe arterial injury in the upper limb was seen. This patient was admitted to St. George Hospital, Sydney, after he had sustained an injury in the left elbow region, disrupting all but one of the branches of the brachial artery. The advisability of amputation was considered before it was decided to attempt to reestablish the blood supply. This was done, with the use of a vein graft. As blood-vessel grafting in the upper extremity is not common, the procedure is reported.

Clinical Record.

Mr. X, aged 50 years, fell out of a motor boat on October 12, 1958. He was struck by the propellor, and among the many injuries he received was a wound across the flexor aspect of the left elbow. In the depths of the wound was a fracture-dislocation of the elbow joint, with separation of the capitellum. More superficially, the proximal ends of the radial and ulnar arteries had been destroyed. The radial and posterior interosseous nerves had been divided, and with them the profunda brachii artery. The supratrochlear artery had also been destroyed. The median and ulnar nerves were still intact. Subsequent arteriography showed that the ulnar collateral artery remained intact. This vessel was apparently inadequate because the hand was blue, cold and anæsthetic at the time of his admission to hospital. A decision was made to attempt arterial repair in this case.

The elbow dislocation was first reduced and the joint stabilized by the capitellum being fixed in position with a "Vitallium" screw. An end-to-end anastomosis of the radial artery was then attempted. A segment of this artery had been destroyed, however, and the ends could not be brought together. An incision was then made at the left ankle and the long saphenous vein was exposed.

A three-inch length of this vessel was removed from between ligatures and transferred to the left elbow region. The brachial artery bifurcation was excised and the distal end of this vessel was cleared of adventitia. The open end of the radial artery was divided cleanly and also stripped of its adventitia. There now remained a gap of about three inches between the brachial artery termination and the radial artery commencement. Into this gap the vein graft was laid, taking care to reverse it so

that any valves present would not interfere with blood flow. At each end of the graft an end-to-end anastomosis was performed; 6/0 black silk on atraumatic curved needles was used for this procedure. The Carrel type of technique was used—intima-to-intima apposition with three equidistant stay sutures being the first step in each anastomosis. Two interrupted sutures were then placed in each interval between the stay sutures. Thus each anastomosis was made with a single layer of nine interrupted sutures. No anticoagulants were used. On removal of the pneumatic cuff from the arm, the graft filled and commenced to pulsate. There was some leakage of blood at each anastomosis, but this stopped completely in about three minutes. It was then noticed that there was a good radial pulse at the wrist and that the hand was pink and warm. Nerve and muscle repair was then performed and the skin wound was partially closed. This closure was completed as a secondary procedure eight days later.

Arteriography was performed at the time of the secondary suture and was repeated four weeks later. The graft was shown to be patent on both occasions (Figure I).[1] At the time of writing, five months after the injury, the left radial pulse is apparently normal and this hand has useful function (Figure II).

FIGURE II.
Photograph indicating the function in the left hand. Wrist drop from a residual radial nerve palsy is apparent.

Summary.

A case illustrating the use of a piece of saphenous vein as an arterial substitute in the upper limb is described.

Reviews.

Cardiac Arrest and Resuscitation. By Hugh E. Stephenson, Jr., M.D; 1958. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Limited. 9¾" × 6¾", pp. 380, with 31 illustrations. Price: £6 12s.

IN recent years it has become increasingly recognized that, under many circumstances, cardiac arrest in the operating theatre is a reversible condition. The volume under review assembles most of the known facts in regard to the causes and treatment of cardiac arrest. Much of the material has been obtained from a Cardiac Arrest Registry set up by the author, through which he obtained details of 1710 cases of cardiac arrest. Where his own knowledge in special branches was deficient, the author has called upon expert help. This has resulted in some slight repetition, but it in no way detracts from the value of the book. Cardiac arrest fortunately is a rare occurrence; but when it does occur, the outcome depends almost entirely on the speed and efficiency with which it is treated. Accordingly this book should be studied by every medical person likely to encounter a case of cardiac arrest. This includes not only all surgeons and anæsthetists, but in addition radiologists and physicians performing intracardiac manipulations. In fact, most doctors would benefit from a careful reading of the volume. It is useless to keep such a book on a library shelf, to be sent for in a case of emergency. The precious minutes and hence the life of the patient can be saved only by a widespread dissemination of the methods set out in this book.

Some idea of the immense amount of work involved in preparing this publication can be obtained from the fact that the bibliography covers 52 pages and lists some 1800 papers. A considerable amount of personal experience and experiment is quoted throughout the book, but never in such a way as to suggest that differing opinions are necessarily wrong.

Though it is useless to wait for a case of arrest before reading this book, nevertheless the unfortunate surgeon who has successfully restarted a heart will obtain a great deal of assistance from the chapters dealing with post-resuscitation care and prognosis. In this section of the book, one deficiency noted is the scant reference to the use of hypothermia in the treatment of the post-resuscitation patient. The method is dismissed with the following sentence: "Recently the immediate application of generalized hypothermia to the patient, following cardiac arrest, has indicated rather startling results in the prevention of permanent or transient neurological sequelæ." This statement appears to be sufficiently "startling" to warrant a more detailed discussion.

This book should be on the shelves of every medical library, as it is likely to be the standard text on this important subject for some time to come.

Applied Anatomy for Nurses. By E. J. Bocock, S.R.N., S.C.M., D.N., and R. Wheeler Haines, M.B., D.Sc., F.L.S.; Second Edition; 1959. Edinburgh and London: E. & S. Livingstone Limited. 8½" × 5½", pp. 338, with 326 illustrations. Price: 17s. 6d. (English).

THIS second edition is a clearly-written, well-illustrated book dealing with the elementary histology, the macroscopic and functional anatomy and some of the physiology of the human body. Attractively presented, it has the occasional opening for criticism. Perhaps a better arrangement of chapters to obviate including together the arm, epithelia and glands, or the eye and autonomic system, would be an improvement.

The book has a number of good figures, including some illustrating the action of muscles, and altogether gives a relatively clear and concise picture of most of the regions of the body. It constitutes a good addition to the nurses' library.

The Epidemiology and Control of Malaria. By George Macdonald, C.M.G., M.D., F.R.C.P.; 1957. London, New York and Toronto: Oxford University Press. 8½" × 5½", pp. 272, with 17 illustrations. Price: 54s. 6d.

THE epidemiology of malaria has been discussed by a great number of authors. From these writings have emerged a mutiplicity of factors which influence the three primary elements concerned in the disease: the mosquito vector, the malaria parasites and the human host.

Attempts at mathematical analysis of malaria epidemiology made by Ross, Waite, McKendrick, Lotka and others were not fully successful. Macdonald examined the premises of earlier workers, and found that they implied that superinfection did not occur. When he adopted the premise that this phenomenon did occur, as indeed it is seen to do in experiment and in nature, he was able to construct a model which allowed him to build up a complete picture of the epidemiology of malaria. Now he has gone further; he has examined the theory of control of malaria. His results have put the present world-wide attack on the disease on a very sound scientific basis—so much so that this effort is now directed towards the foreseeable eradication of malaria from the world.

From these studies have emerged the basic significant factors involved in the epidemiology of malaria. Amongst these, one of considerable importance is the expectation of life of the particular anopheline vector in the area. This has led to a number of studies to construct life tables for anopheline species by determining the age distributions of anopheline populations. It was found that more exact information was required to do this precisely. The work of Detinova in Russia and of Gillies in Tanganyika may be noted in this field. Other important factors include the number of the vector's infective feeds per day, the sporozoite rate in the vector and environmental tempera-

[1] For Figure I see art-paper supplement.

ture. From these Macdonald has developed the concept of stable and unstable malaria—the former being much more difficult to control than the latter.

Here, then, is a mathematical model which can be tested and refined. It has demonstrated the important factors to be considered in explaining the local variations in malaria epidemiology, and has concentrated studies in these critical fields. The book is an endeavour to explain in colloquial form the concepts derived from mathematical techniques. How far the author has succeeded will mostly depend on the extent to which the reader is willing to exert himself. It is a book to be studied, not only by the malariologist, but also by epidemiologists in general.

The Principles and Practice of Electrotherapy and Actinotherapy. By Bryan O. Scott, M.R.C.S., L.R.C.P., D.Phys.Med.; 1959. London: William Heinemann Medical Books Limited. 8½" × 5½", pp. 322, with 168 illustrations. Price: 27s. 6d. (English).

THIS book has been designed as a text in medical electricity for physiotherapy students, and covers the syllabus for examinations conducted by the Chartered Society of Physiotherapy in Great Britain. There is, therefore, no reference to long-wave diathermy, which has been dropped from the syllabus for the examination. This seems perhaps a pity when many such machines are still in use.

The first hundred pages of the book deal adequately with elementary physics as applied to the subject. Low-frequency currents are dealt with briefly, and there is a concise, but very clear, account of electrical stimulation and electrodiagnosis.

The reasons given by the author for omitting the usual motor-point charts for stimulation do not seem to justify the exclusion of a chart which is most useful to students.

Short-wave diathermy receives a chapter to itself; but no mention is made of possible damage to hearing aids, which is a matter of medico-legal importance, and scant attention is given to the operating circuit of the machine.

It would also be helpful for students if some form of list of indications could be mentioned for short-wave treatment, even though, as the author quite rightly points out, we are treating a lesion rather than a disease. It is pleasing to see the brief but adequate reference to micro-wave and ultrasonics.

A chapter is devoted to the dangers of electrical treatment, including earth shocks, but there is inadequate reference to earth-free currents.

The last one hundred pages are devoted to actinotherapy; but the only chart of the electromagnetic spectron is calibrated entirely in metres. The usual method of using metres and Ångström units seems preferable.

The book is clearly printed and illustrated, and should prove most useful as a modern text in the subject for physiotherapy students. It is, however, rather too condensed and elementary to prove of much value as a reference work for experienced practitioners.

The Psychiatric Aide: A Textbook of Patient Care. By Alice M. Robinson, R.N., M.S., foreword by Walter E. Barton; Second Edition; 1959. Philadelphia and Montreal: J. B. Lippincott Company. Sydney: Angus and Robertson, Limited. 8" × 5", pp. 226, with illustrations. Price: £1 18s. 6d.

THIS book is clearly written by a person with sound practical experience and a healthy respect for the staff who spend "the other twenty-three hours" with the psychiatric patient in hospital. Again and again, in various ways, stress is placed on the importance of interpersonal relationships and communication, and on the need to study the individual patient's needs and behaviour; thus is formed the basis of a satisfactory therapeutic atmosphere within the patient groups, the ward and the hospital.

The dynamics of human behaviour are discussed, particularly as these affect patient behaviour and patient and patient-staff reactions. The basic need for the nurse to be a warm and friendly person, to be trustworthy, dependable and consistent at all times, and to respect his or her patients as fellow human beings, is recognized. The importance of an awareness of staff feelings and reactions, and the need to cultivate the ability to do something about these when necessary, are emphasized.

The special contributions of the psychiatrist, social worker, psychologist and recreational and occupational therapist, and the role of the nurse and aide in relation to the team, are made clear.

The specific duties and perhaps more time-honoured responsibilities of the nurse and aide, in regard to the physical care of patients and the day-to-day domestic ward routines, are not overlooked; but here again the importance of personal contacts with both patients and staff is emphasized. The need to foster a "family group" and to make every effort to make the ward a "home" receives timely attention.

In discussing electrotherapy and full coma insulin techniques, no attempt is made to lay down rigidly detailed duties for the nurse or aide. The author points out that these duties will differ in details from hospital to hospital and will be taught "on the job". The nurse's role in supporting and reassuring patients in this situation is discussed. The management of the various emergencies, such as suicidal attempts, aggressiveness and fire, is treated in accordance with modern trends.

Special sections are given to the geriatric patient, ataractic drugs, activities programmes for open wards and convalescent patients, ethical obligations, group and individual psychotherapy, the organization of ward routines and the management of various behaviour difficulties. No attempt is made to elaborate diagnostic classifications. Stress is laid on the inherent dangers of "labelling" or attempting to "pigeonhole" patients. The nurse is urged to view her patients as sick "individuals", each of whom she should learn to know "as a person". She is urged to become acutely aware of "the ways of human beings", including herself.

Although it is written primarily for the American psychiatric aide, this book should be read by all who are interested in the care of the psychiatric patient. It will be of particular use to nurses, aides and ward administrators, but will be readily understood by interested laymen and very helpful to relatives. Jargon is avoided, and the book is written in a clear and direct style which should appeal to all. Within the limits indicated it is an excellent presentation of modern and up-to-date psychiatric nursing.

Food Inspection Notes: A Handbook for Students. By H. Hill, F.R.S.H., F.S.P.H.I., A.M.I.P.H.E., and F. Dodsworth, F.R.S.H., F.S.P.H.I., M.Inst.P.C.; Fifth Edition; 1959. London: H. K. Lewis & Company, Limited. 6½" × 4", pp. 128. Price: 10s. 6d. (English).

THIS neat little book contains a section on inspection of meat and smaller sections on inspection of poultry, rabbits, game, fish, shell fish, milk, milk products and canned foods. Brief references to the inspection of many other foods are grouped together in a separate section.

Bacterial food poisoning is summarized under the headings "Causative Organisms", "Symptoms", "Mode of Infection", "Food Affected" and "Investigations". Other types of food poisoning are not mentioned. A brief outline of food sampling, a comprehensive bibliography and an index then follow.

This handbook for students is descriptive, yet concise in its presentation. The student will appreciate the manner in which the text is handled. The various aspects of food inspection are grouped together in a manner that will greatly assist the assimilation of a reasonably large range of subject material. The authors, in condensing these notes from many English and international authorities, have not overlooked the necessity of conveying to the reader the important features relative to food inspection work in simple phraseology.

It is interesting to see the variations of slaughtering and inspection techniques existing in the United Kingdom. Since the book is an English publication, certain features which are mentioned with some degree of importance in relation to local conditions are either not practicable or of minor consideration in Australia and vice versa.

The article on hydatid cysts deals with hydatid disease on a general scale. It is of considerable importance in Australia, and would have received more attention in an Australian textbook. *Echinococcus granulosus*—the hydatid tapeworm—is referred to as *Tænia echinococcus*.

The section dealing with inspection of fish is of a wide coverage; but unfortunately some of the varieties are not seen or are known by other names in this country.

From the viewpoint of the student and the practising food inspector, the whole book is an excellent reference, condensed into note form and published in such a size that it can be easily carried in a suit-coat pocket. It deals with all the aspects of food inspection that the student is expected to know. It is practical and authoritative, and should be welcomed by the professional person and the student alike.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"A Study in Right Heart Performance in Man with Special Reference to the Effect of Experimentally Induced Acute Hypervolemia", by Bengt Thomasson; The Scandinavian Journal of Clinical and Laboratory Investigation, Vol. 11, Supplmeent 40; 1959. Stockholm: Tryckeri Balder. 9¼" × 7", pp. 76, with illustrations. Price: not stated.

"Coronary Heart Disease", by John William Gofman, M.D., Ph.D.; 1959. Oxford: Blackwell Scientific Publications. 9" × 6", pp. 378, with 52 tables. Price: 60s. (English).

"Genetics, Radiobiology and Radiology Proceedings, Mid-Western Conference", by Wendell G. Scott, M.D., and Titus Evans, Ph.D.; 1959. Oxford: Blackwell Scientific Publications. 9" × 6", pp. 166, with 10 illustrations. Price: 42s. (English).

"Water Supply for Rural Areas and Small Communities", by E. G. Wagner and J. N. Lanoix; World Health Organization Monograph Series, No. 42; 1959. Geneva: World Health Organization. 9" × 6", pp. 340, with 85 illustrations. Price: £1 15s.

"Papers Dedicated to Dr. Kjeld Tørning on his Sixtieth Birthday, June 29, 1959", Acta Tuberculosea Scandinavica, Supplement 47; 1959. København: Ejnar Munksgaard. 10" × 6¾", pp. 242, with many illustrations and tables. Price: not stated.

"A Clinical Study of the Hæmagglutination Reaction in Tuberculosis", by Jan Spangberg; 1959. Copenhagen: Ejnar Munksgaard. 10" × 6¾", pp. 96, with many tables. Price: not stated.

"Proceedings of the Nineteenth Scandinavian Congress for Pulmonary Diseases in Turku (ABO), August 7-9, 1958", edited by Risto Lahesmaa; 1959. Copenhagen: Ejnar Munksgaard. 10" × 6¾", pp. 134, with illustrations and tables. Price: not stated.

"Hale-White's Materia Medica, Pharmacology and Therapeutics", edited by A. H. Douthwaite, M.D., F.R.C.P. (Lond); thirty-first edition; 1959. London: J. & A. Churchill, Limited. 7¼" × 4½", pp. 536. Price: 25s. (English).

"Surgical Service Guide", by Louis T. Palumbo, M.D., M.S., F.A.C.S.; 1959. Chicago: The Year Book Publishers, Inc. Sydney: W. Ramsay (Surgical) Limited. 7¾" × 5", pp. 208, with illustrations. Price: 66s.

"Teach Yourself to Relax", by Josephine L. Rathbone, Ph.D.; 1959. Sydney: Angus & Robertson, Limited. 8" × 5¼", pp. 232, with illustrations. Price: 26s. 6d.

"Synopsis of Treatment of Anorectal Diseases", by Stuart T. Ross, M.D., F.A.C.S., F.I.C.S.; 1959. St. Louis: The C. V. Mosby Company. Sydney: W. Ramsay (Surgical) Limited. 7¼" × 4½", pp. 240, with 79 illustrations. Price: £3 11s. 6d.

"Synopsis of Ear, Nose, and Throat Diseases", by Robert E. Ryan, B.S., M.D., M.S. (Alr.), F.A.C.S., William C. Thornell, A.B., B.M., M.D., M.S. (Alr.), F.A.C.S., and Hans von Leden, M.D., F.A.C.S., F.I.C.S.; 1959. St. Louis: The C. V. Mosby Company Sydney: W. Ramsay (Surgical) Limited. 7¼" × 4½", pp. 383, with 59 illustrations. Price: £3 14s. 3d.

"Forensic Medicine: Observation and Interpretation", by A. Keith Mant, M.D. (Lond.); 1960. London: Lloyd-Luke (Medical Books) Limited. 8½" × 5½", pp. 272, with 118 illustrations. Price: 42s. (English).

"Maternal Disorders: Related to Fetal Stress, Perinatal Death and Congenital Defects", Selected References 1952-58; compiled by Elizabeth Koenig; 1959. Washington: U.S. Government Printing Office. 9" × 5¾", pp. 40. Price: 15 cents.

"Communicable Diseases in Schools: A Survey of Existing Legislation", offprint from World Health Organization: International Digest of Health Legislation, Geneva, Vol. 10, No. 2; 1959. 9½" × 6¾", pp. 66. Price: 3s. 6d. (published in English and in French).

"The Care of Minor Hand Injuries", by Adrian E. Flatt, M.A., M.D., F.R.C.S., with a foreword by Carroll B. Larson, M.D.; 1959. St. Louis: The C. V. Mosby Company. Sydney: W. Ramsay (Surgical) Limited. 9¾" × 6¾", pp. 266, with 109 illustrations. Price: £5 4s. 6d.

"More Medical and Other Verses", by Alex. E. Roche; 1959. London: H. K. Lewis & Company, Limited. 7¼" × 4½", pp. 43. Price: 5s. (English).

"Surgery of the Foot", by Henri L. DuVries, M.D., foreword by Karl A. Meyer, M.D., introduction by Edward L. Compere, M.D.; 1959. St. Lous: The C. V. Mosby Company. Sydney: W. Ramsay (Surgical) Limited. 9¾" × 6¾", pp. 494, with 403 figures. Price: £6 17s. 6d.

"Anesthesia for Infants and Children", by Robert M. Smith, M.D., foreword by Robert E. Gross, M.D.; 1959. St. Louis: The C. V. Mosby Company. Sydney: W. Ramsay (Surgical) Limited. 9¾" × 6¾", pp. 418, with 182 illustrations and 37 tables. Price: £6 12s.

"Therapeutic Radiology: Rationale, Technique, Results", by William T. Moss, M.D., with foreword by Lauren V. Ackerman, M.D.; 1959. St. Louis: The C. V. Mosby Company. Sydney: W. Ramsay (Surgical) Limited. 9¾" × 6¾", pp. 403, with 146 illustrations. Price: £6 17s. 6d.

"Clinical Neurosurgery: Proceedings of the Congress of Neurological Surgeons, San Francisco, California, 1958"; 1959. Baltimore: The Williams & Wilkins Company. 9" × 5¾", pp. 310, with many illustrations. Price: £6 1s.

"Neurology of Infancy", by Anatole Dekaban, M.D., Ph.D.; 1959. Baltimore: The Williams & Wilkins Company. Sydney: Angus & Robertson, Limited. 10" × 6¾", pp. 402, with 185 illustrations. Price: £6 12s.

"Atlas and Manual of Dermatology and Venereology", by Professor Dr. W. Burckhardt, translated and edited by Stephan Epstein, M.D.; 1959. Baltimore: The Williams & Wilkins, Company. Sydney: Angus & Robertson, Limited. 9¼" × 6¾", pp. 302, with 99 colour plates and 73 black and white illustrations. Price: £7 14s.

"Doctors and Patients: Stories by Leading American Physicians", edited by Noah D. Fabricant, M.D.; 1959. New York and London: Grune & Stratton, Incorporated. 9" × 5¾", pp. 224. Price: $5.25.

"Doctors' Commons: A Short History of the British Medical Association", by Paul Vaughan; 1959. London, Melbourne and Toronto: William Heinemann, Limited. 8¼" × 5½", pp. 274, with illustrations. Price: 22s. 6d.

"Annotated Bibliography of Filariasis and Elephantiasis: Part 3, Symptomatology, Ætiology, Pathology and Diagnosis of Filariasis Due to Wuchereria Bancrofti and W. Malayi", by M. O. T. Iyengar; South Pacific Commission Technical Paper No. 109 (Supplement No. 1); 1959. Noumea, New Caledonia: South Pacific Commission. 10" × 8", pp. 30. Price: 2s. (sterling).

"The Year Book of Medicine (1959-1960 Year Book Series)", edited by Paul B. Beeson, M.D.; Carl Muschenheim, M.D.; William B. Castle, M.D.; Tinsley R. Harrison, M.D., Franz J. Ingelfinger, M.D., and Philip K. Bondy, M.D.; 1959. Chicago: The Year Book Publishers, Incorporated. Sydney: W. Ramsay (Surgical) Limited. 7½" × 4¾", pp. 732, with 110 illustrations. Price: 88s.

"Mental Health in the Light of Ancient Wisdom", by Henry V. Dicks, M.A., M.D., F.R.C.P.; The First Mary Hemingway Rees Memorial Lecture, Vienna, 1958; 1959. London: H. K. Lewis & Company, Limited for the World Federation for Mental Health. 8½" × 5½", pp. 24. Price: 2s. 6d. (English) (paper cover).

"Histonomy of the Cerebral Cortex", by S. T. Bok; 1959. Amsterdam, London, New York and Princeton: Elsevier Publishing Company. London: D. Van Nostrand Company, Limited. 8¾" × 5¾", pp. 446, with 176 illustrations. Price: 72s. (English).

"Napoleon Immortal: The Medical History and Private Life of Napoleon Bonaparte", by James Kemble, Ch.M., F.R.C.S.; 1959. London: John Murray, Limited. 8½" × 5½", pp. 320, with illustrations. Price: 28s. (English).

"Aldosterone in Clinical and Experimental Medicine", by E. J. Ross, M.D., Ph.D., M.R.C.P.; 1959. Oxford: Blackwell Scientific Publications, Limited. 8¾" × 5½", pp. 152, with 5 tables. Price: 22s. 6d. (English).

"A Guide to Antibiotic Therapy", by Henry Welch, Ph.D.; 1959. New York: Medical Encyclopedia, Incoporated. 10" × 6½", pp. 72. Price: $3.00.

"Fear, Punishment Anxiety and the Wolfenden Report", by Charles Berg; 1959. London: George Allen & Unwin, Limited. 8½" × 5¼", pp. 128. Price: 20s. (English).

"Clinical Chemical Pathology", by C. H. Gray, D.Sc., M.D., M.R.C.P., M.R.C.S., F.R.I.C.; second edition; 1959. London: Edward Arnold (Publishers) Limited. 7¼" × 4¾", pp 168, with 28 figures. Price: 26s.

The Medical Journal of Australia

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DOCTORS WITHOUT CREDENTIALS.

Two THINGS are normally required of a doctor if he desires the full status of his profession: adequate training, and some tangible evidence to establish the fact of this training and his good character—in other words, his credentials. Without these credentials he may find himself frustratingly precluded from applying his training, no matter how good it may have been. This is not unreasonable. As Professor Edward Grzegorzewski[1] has stated, the doctor occupies a position of peculiar trust in relation to his patient, one of intimacy and mutual confidence, essential to the exercise of his profession and readily accorded to him by his patients and by the community at large. Not unreasonably, from early times various means have been devised to safeguard this position in the interests of patient, doctor and community. The medical profession itself has always exercised a degree of control over its members in this regard. Then the community or the ruling authorities took a hand, and in most modern countries statutory bodies exist for purposes of registration and supervision. In addition, universities and other institutions of higher learning have exercised their influence and authority in the establishment of standards of training. The proportion and nature of the responsibility of each of these three elements differ in accordance with the social structure and other cultural characteristics of the country, Professor Grzegorzewski points out, but in one way or another the government, the educational institutions and the medical professional bodies between them can assure the population that its medical care is provided by properly qualified persons. "Each of the groups serves as a channel of public trust, and thus derives its power not from itself, but from the interest of the people of the community." It is in that interest that medical credentials are issued, indicating that the medical man has complied with the requirements laid down, has accumulated sufficient knowledge of medicine and is qualified to apply it at his discretion within the existing legal, ethical and administrative norms.

Occasionally, cheap sneers are heard about the licensing of doctors and about the bodies responsible for such licensing, but these may be dismissed. It is in the interests of everybody, including the doctor, that such control should be exercised, and the doctor loses nothing in dignity from being formally accepted into a respected group of established status. His worries begin when he finds himself in a strange land without his credentials, as has happened to many of our colleagues as the result of, for example, the second World War and the more recent incidents in Hungary. No matter what one's training and standing have been, it is difficult to establish one's status amongst strangers without objective evidence. Certainly in Australia credentials are regarded as of the utmost importance, as will be seen from the special article on the subject published elsewhere in this issue (see page 226).

In 1948, Dr. Jean Maystre records,[2] the World Medical Association was informed that the United Nations were caring for more than 1500 displaced physicians, most of whom had no way of proving that they were qualified as medical doctors. They were doctors without credentials. Their identification required a great deal of investigation and trouble which could have been avoided had their diplomas been saved. As a result of this experience, W.M.A. set about organizing a Central Repository for Medical Credentials to ensure the protection of the medical credentials of all those who cared to take advantage of it. The facilities of the repository became available on July 1, 1958 (we published details at the time),[3] and are open to every doctor who is qualified to practise medicine. It is suggested that the following credentials warrant protection: (i) transcripts of pre-medical and medical school records; (ii) medical school diplomas; (iii) registration certificates from state or national boards; (iv) certificates of specialities; (v) post-graduate diplomas and honorary degrees. The repository will accept medical credentials in the following forms: (i) photostat copies of originals; (ii) microfilm copies of originals; (iii) authenticated copies of originals; (iv) official medical school transcripts; (v) originals. The applications, credentials and identification papers, signed in the presence of qualified witnesses, must be transmitted to W.M.A. through the appropriate member national medical association. Special application and identification forms may be obtained from the secretariat of the member associations. The administration of the Central Repository Service is in the hands of the Headquarters Secretariat of W.M.A. A fee is charged which averages for the different age groups about two dollars a year for life-time protection. Paid in one instalment the life-time cost for the newly-graduated doctor is approximately $60.00. An actuarial schedule has been established for doctors in the various age groups. A ten-year service rate is also available. The fee has been kept as small as is compatible with providing the essentials of the service.

The response to this opportunity has apparently been much smaller than was anticipated. Most doctors would agree that the idea was sound; but it is another matter to do something about it. No doubt the fee deters some. In Australia we may well be thinking that if disaster came to this part of the world of such magnitude that we would wish to flee elsewhere, there would scarcely be anywhere to go to. There is undoubtedly a good deal of

[1] *World med. J.*, 1959, 6:107 (March).

[2] *World med. J.*, 1959, 6:116 (March).

[3] MED. J. AUST., 1958, 2:96 (July 19).

truth in this, but we would be wise to think very hard before making it the only consideration determining our attitude to the Central Repository.

Current Comment.

REPORT OF THE BRITISH EMPIRE CANCER CAMPAIGN.

THE thirty-sixth annual report of the British Empire Cancer Campaign covering the year 1958 has now been published.[1] As in former reports much information is given regarding the constitution of carcinogens, and the list of these is extended. Some experiments on the intracellular distribution of polycyclic hydrocarbons indicate that possibly carcinogens, unlike non-carcinogens, penetrate the cell nuclei.

In each annual report there can be found accounts of improvements in technical methods, physical and biological, which can be put to good use in other fields than cancer research. Thus in this 1958 report details are given of a method of protein analysis which is certain to be extensively applied in a large number of biochemical and immunological investigations. A preliminary salt fractionation is used before chromatography with carboxymethyl cellulose. The results are most promising.

One of the most interesting finds is as follows. Hens were kept in unvarying illumination and in unvarying temperature and humidity. Malignant tumours in oviducts and ovaries were observed far in excess of those in normal control hens. It is suggested that absence of climatic fluctuations leads to long periods of reproductive activity without those intermissions which moulting and new feather growth impose, and that this sustained reproductive activity may be the cause of the malignancy or predisposition to malignancy. That cancer, at least in the human being, is connected with the reproductive system has long been surmised.

One experiment is open to criticism. The nipples of 20 mice were excised on one side; after which mating, pregnancy and lactation followed. Carcinogen was then painted on the skin covering both rows of mammary glands during lactation; it was found that cancer developed on the non-suckable side far in excess of that on the suckable side. The suggestion is made that lactation removes carcinogen, but the authors do not discuss the possibility of the irritation produced by unrelieved back pressure tilting the balance over into malignancy. Elsewhere it is pointed out that the activity of the liver in removing cancer cells introduced by the portal blood is inhibited if a laparotomy is carried out. In this connexion the authors might have mentioned the fact, well known in veterinary science, that the udder of dairy cows, surely an abnormal structure, rarely shows malignancy.

As usual an enormous field is covered, and although the central problem of cancer remains unrevealed, the work done must be of use in other departments of biological science.

LIVE POLIOVIRUS MASS VACCINATION IN THE SOVIET UNION.

AN interesting report has been received from the World Health Organization of a mass vaccination programme against poliomyelitis begun in the Soviet Union in 1959 using a live-virus vaccine given by mouth. Ten million persons had already been vaccinated when the report was prepared; 15 million were to be vaccinated by January, 1960, and it is planned that, by the end of 1960, 88 million persons will have been vaccinated, including the entire population of the Soviet Union under the age of 20 years. The vaccination used in the U.S.S.R. is made from virus strains supplied by A. B. Sabin of Cincinnati, U.S.A.

In agreement with the Soviet Ministry of Health and the United States Public Health Service, WHO recently invited the distinguished American scientist, Dr. Dorothy M. Horstmann, to visit the Soviet Union in order to evaluate the safety and efficiency of the new vaccination against poliomyelitis. Dr. Horstmann, who is Associate Professor of Preventive Medicine and Pediatrics at the Yale School of Medicine, stayed in Moscow, Leningrad, Tashkent and Riga and then visited Poland and Czechoslovakia, where live poliovirus vaccine is also being used. According to her report, the marked reduction in incidence of poliomyelitis in the Soviet Republics where oral vaccination has been applied suggests that the vaccination has played a significant role in reducing the incidence of paralytic poliomyelitis. Compared with the pattern of rising incidence over the past few years, the low 1959 incidence in the U.S.S.R. is impressive. Dr. Horstmann states, however, that at least another year is needed before a valid judgement can be made about the effectiveness of the vaccine.

In January, 1959, vaccination was offered on a voluntary basis by the central government to all the Soviet Republics. The Estonian Minister of Health was the first to ask for it. Lithuania, Kazakhstan, Uzbek and the other republics followed. The plan of vaccination has varied in the different republics. In Georgia, for example, the vaccine was put up in candy balls about one centimetre in diameter and tested first on a small group of children with satisfactory results. Dr. Horstmann praises the Soviet scientists working on the programmes as highly skilled and states that standards of laboratory work are good. Surveillance of poliomyelitis in the U.S.S.R. she describes as very good. Detailed records are kept, and the Ministry of Health in Moscow has set up a special notification system under which local physicians make an immediate report on any new case of poliomyelitis to regional and centralized offices. Chief scientist for the Soviet programme is Dr. M. P. Chumakov. When the inhabitants of a new region are to be vaccinated, Dr. Chumakov and his staff go there to meet the local doctors and participate in the drive to explain the vaccination campaign to the public.

In Poland, Dr. Horstmann reports, the vaccination programme is well organized, surveillance of cases is good, and laboratory work meets accepted standards. It should be possible to have accurate information relatively soon on the results of mass vaccination in terms of safety and, over the next few years, in terms of effectiveness. On her visit to Czechoslovakia, Dr. Horstmann states that the excellent and well-controlled trials in that country have provided valuable data on the safety of the Sabin vaccine in Salk-vaccinated communities, and that continuing studies on the fate of the poliovirus vaccine strains in these communities are of the greatest interest.

THE VALUE OF ELECTROCARDIOGRAPHY IN SUSPECTED CORONARY ARTERY DISEASE.

MUCH doubt exists as to the value of electrocardiography in the diagnosis and prognosis of coronary artery disease. J. W. Todd[1] has reviewed and analysed the problem. He points out that the symptoms of angina pectoris and angina of effort are quite well defined and can be elicited only by talking to the patient. The electrocardiogram can neither confirm nor deny that the typical pain is felt. When, as is usual, the angina is due to coronary artery disease, the electrocardiogram is sometimes normal, and sometimes reveals various abnormalities, such as left axis deviation or evidence of old infarction or of bundle branch block. The electrocardiogram which is normal at rest may become abnormal after

[1] "British Empire Cancer Campaign: Thirty-Sixth Annual Report Covering the Year 1958"; 1959. London: British Empire Cancer Campaign. Part I: The Chairman's Statement and the Accounts. 9¾" × 7½", pp. 42. Part II: The Scientific Report. 9¾" × 7½", pp. 650, with illustrations.

[1] *Lancet*, 1959, 1: 845 (April 25).

the patient has exercised, but it may not. Many investigations have shown that the prognosis is worse when the electrocardiogram is abnormal than when it is normal, but there is not sufficient information to determine whether the nature of the electrocardiographic abnormality affects the prognosis. Recurrent attacks of precordial pain or discomfort not related to effort and without the typical distribution of angina pectoris are not uncommon, and here an abnormal electrocardiogram undoubtedly favours the diagnosis of coronary artery disease, but it does not make the diagnosis certain. Where there are emotional cardiac disturbances associated with precordial pain, the electrocardiogram is valueless in aiding the diagnosis. On the other hand, it is very wrong to deduce that a patient cannot have angina of effort because an electrocardiogram, even after exertion, is not abnormal, and that the patient must be neurotic.

When cardiac infarction is suspected, the electrocardiogram is of undoubted value. But it does not follow that because fatal myocardial infarction nearly always causes characteristic electrocardiographic changes, the same is true of non-fatal infarction. There is no way of proving that a patient has not had a non-fatal cardiac infarction. When the patient is desperately ill, the diagnosis matters comparatively little, for the initial treatment is little affected by the diagnosis.

Undoubtedly very large numbers of minor infarcts are not diagnosed at the time, and there is no clear evidence that harm results from lack of diagnosis where the patient has transient pain and shows little or no shock or congestive failure or other symptoms. There appears to be no good evidence that the electrocardiographic findings can legitimately modify the opinion of the severity of the process which has been reached on clinical grounds. Todd deprecates the routine electrocardiography practised in industrial organizations in the United States. The vast numbers of workers involved, both executives and ordinary employees, have their regular electrocardiographic examinations among other examinations. As a result of these, men are retired or transferred to other work even though there is no other evidence that the individual is not fully capable and will not necessarily die early. This can lead to compulsory unemployment at the worst and considerable worry at the best. A normal electrocardiogram is no proof that the heart is functioning well in the absence of symptoms. Todd quotes an investigation carried out by L. G. Davies[1] in which 100 electrocardiograms were given to 10 skilled observers, to report as to normality, the presence of infarction or abnormality. This was repeated later. Complete agreement was reached on only one-third of the tracings and majority agreement on half. There was considerable dispute about one-fifth of the tracings. In the second reading each observer, on average, disagreed with one in eight of his orginal reports. Obviously, except when the electrocardiographic changes are considerable, the diagnosis is of little value but can lead to much trouble. Todd concludes that "electrocardiography has been greatly overvalued in the investigation of patients with suspected coronary artery disease" and comments: "Electrocardiography cannot help in deciding whether or not a patient has angina of effort. It is of small or doubtful value in determining both ætiology and prognosis when angina is present."

[1] *Brit. Heart J., 1958, 20: 153.*

OLD AGE AND MENTAL HEALTH.

DEAN SWIFT was a misanthropist whose biting sentences have, in many places, revealed to us the shortcomings of our race, but surely nowhere has his warped genius given us a more telling and pitifully accurate picture than his account of the Struldbrugs seen by Gulliver during his third voyage. Need old age always bring this combination of mental failure, physical infirmity and social ostracism? A recent WHO publication[1] examines this question in regard to mental health.

This excellent and readable technical report is notable not so much for the light it sheds on the origins of mental disease in old age, but rather for the well-balanced discussion on steps that may be taken to deal with the problem. The WHO committee lays emphasis on the intricacy with which medical, social and mental problems are interwoven in old age. To deal with this it strongly recommends the establishment of geriatric guidance centres as an integral part of the services of a general or mental hospital. It points out that by this means the imperative demands for coordination of services are met, and that the incidental difficulties of staffing and maintaining high standards of treatment among geriatric patients are avoided by having available the whole services of the general hospital.

The report gives a list of important points, on which research is needed, and this is surprisingly wide in scope. It appears, for instance, that very little is known regarding the relation of social environment to the hazard of becoming mentally ill in old age. It is likewise interesting to know that few investigations of genetic factors have yet been carried out. Perhaps the hypothesis put forward by Leo Szilard[2] regarding chromosomal mutations may stimulate work on this line.

Mental disease in old age is more than a matter for psychiatrists in psychiatric institutions. As all intelligent people are aware, it is more than a matter for the medical profession alone, since its effects can be felt in everyday life—in business management, behind the driver's wheel and in the family circle. That the WHO committee recommends strong measures to deal with the problem is but another indication of the excellent work being performed by this body. The recommendations do the subject no more than justice.

[1] "Mental Health Problems of Ageing and the Aged", W.H.O. Technical Report No. 171, Geneva, 1959.

[2] *Proc. nat. Acad. Sci.*, 1959, 45: 30 (January).

CRITICISM IN MEDICINE.

WHEN Sir Francis Walshe[1] had critically reviewed some of Wilder Penfield's notions of the function of the cerebral cortex, Penfield[2] said in his reply that polemic writing had little virtue and brought no benefit to medical science. Writing recently in a new medico-philosophical quarterly, Walshe[3] suggests that if Penfield is using "polemic" as a pejorative substitute for "critical", this cannot be the mature reflection of a distinguished writer. Walshe goes on to remark that critical thinking may come before us in two ways: first, the individual scientific worker is obliged to apply it to his own work; second, the thinking reader is obliged to apply it to the works of authors who have not fulfilled their obligations. In medicine there is a vast literature of which no one can hope to cover even a fraction. To this, Walshe points out, we have added the symposium fashion; the wandering symposiast contributes the same message to a dozen meetings, each of which produces a volume of "Proceedings".

> To this chorus the not muted voices of the medical statisticians are now added, with their terminology of "double-blind tests" . . . adding impressiveness to our papers with their formulas except when, as has been known to happen, statistical methods have been applied to raw material incapable of refinement by mathematical clarifiers by reason of its confusion.

Criticism, Walshe writes, is dead only in fields of knowledge that are not progressing. In any branch of knowledge which is advancing creation and criticism are equal partners. Destruction of one means the destruction of the other. No scientist should expect to have his papers regarded as infallible utterances before which his colleagues bow in silent homage.

[1] *Brain, 1957, 80: 510 (September).*

[2] *Brain*, 1958, 81: 231 (June).

[3] *Perspectives in Biology and Medicine*, 1959, 2: 197 (Winter).

Abstracts from Medical Literature.

PSYCHIATRY.

Behavioural Response after Frontal Lobe Surgery.

M. GREENBLATT (*Amer. J. Psychiat.*, September, 1959) has studied the relationship between the patient's history, personality and family pattern and behavioural response after frontal lobe surgery in a series of 181 chronic psychotics subjected to lobotomy between 1943 and 1949. Thirty traits were carefully analysed before and after operation. These traits were considered relatively objective, readily observable and easily rated. The most favourable results were obtained in the following areas: food refusal, elated mood, fear, worry, depression, and obsessional compulsive phenomena. Undesirable changes which appeared after leucotomy included alcoholic excess, convulsions, incontinence of urine, over-talkativeness and lack of sociability. In four traits the improvement was overshadowed by the production of undesirable effects. Excessive appetite, irritability, outspokenness and deficient insight are more often produced than reduced by operation. The degree of satisfaction felt as the result of given personality changes after leucotomy is in large measure a function of family dynamics. An increase or decrease in aggressiveness or dominance on the part of the patient pleased some families and in others had the opposite effect. Studies of social interaction showed a considerable dependence of post-operative change on the pre-operative level. In general the tendency was towards a more normal type of behaviour; patients with excessive activity of anti-social type moved towards more socially acceptable behaviour, as did those with a marked deficiency in social activity. As regards the problem of prediction of mental status after operation, it was noted that the best outcome was produced in psychoneurotics rather than schizophrenics, and in those cases in which the following features were present: rapid onset, high tension, presence of insight, absence of hallucinations, "verbalness" and friendliness. The author concludes that the reactions to severe brain cutting are not to be predicted only on the basis of the type and amount of brain cut or destroyed, but in relation to many factors from the background and personality of the patient.

Heller's Disease and Childhood Schizophrenia.

N. MALAMUD (*Amer. J. Psychiat.*, September, 1959) reports the cases of six children, in which the clinical manifestations were those of progressive psychological and neurological deterioration, and as such closely resembled the cases described by Heller. All six proved to be suffering from organic brain disease, but the precise diagnosis was only established at autopsy. The clinical diagnosis of childhood schizophrenia in these examples was due to either ignoring or underestimating the role of organic factors in the total picture, e.g. motor disturbances were considered to be mannerisms. The author comments that the designation of Heller's disease is not sufficiently precise, and can in fact be misleading; not only has it become a waste-basket diagnosis for all sorts of organic brain disease, but, more important, it has been confused with childhood schizophrenia.

Aggression, Guilt and Cataplexy.

M. LEVIN (*Amer. J. Psychiat.*, August, 1959) quotes five brief records of patients who experienced cataplexy following incidents in which their aggression was provoked, and refers to 16 papers in which similar experiences had precipitated attacks. He comments that the aggression may be undisguised as in hunting, fishing and boxing, or it may be symbolic as in those sports where the object is to defeat the opponent but not hurt him. Cataplexy which has followed practical jokes is also included, as the author considers that these are a benign expression of aggression. He comments that in all of these cases the cataplexy is a manifestation of conditioned inhibition, a response to the guilt which attends aggression even when it is only unconscious.

Parents of Schizophrenics, Neurotics, and Normals.

S. FISHER *et alii* (*A.M.A. Arch. gen. Psychiat.*, August, 1959) investigated the question of whether parents of schizophrenics differ significantly from parents of non-schizophrenic patients. The parents of 20 normal men, 20 neurotic men and 20 schizophrenic men were compared by means of a variety of psychological investigations. These included individual interviews, projective questions, Worcester scale of social attainment, thematic apperception test, and parental interaction evaluations. They found that parents of normal individuals are individually less maladjusted than parents of neurotics or schizophrenics, but that there were no apparent differences in this respect between parents of neurotics and parents of schizophrenics. It was also shown that both parents of normal individuals and neurotics may be distinguished from parents of schizophrenics by having closer, more harmoniously intercommunicating spouse relationships.

The Treatment of Delirium Tremens.

H. KRYSTAL (*Amer. J. Psychiat.*, August, 1959) discusses the physiological basis of the treatment of delirium tremens. This discussion is based on an investigation of 700 cases of delirium tremens; in this series there were 17 deaths, and the author studied the water and electrolyte disturbance of 45 of these patients. He concluded that there are at least six clinically recognizable ætiological factors: dehydration, magnesium deficiency, sodium and chloride deficiency, brain swelling, fulminating infection and panic state. The assessment of the contribution which each factor makes is difficult, due to the blending of these symptoms with the non-specific symptoms of delirium. The author states that the patient's chance for survival depends on the application of the principles of specific psychiatric and physiological diagnosis followed by specific rather than routine treatment. Paraldehyde is not favoured by the author, who believes that it achieves the same effect as the intravenous administration of alcohol did in the past: gastritis is circumvented and enough acetaldehyde is supplied to produce the euphoria which the patients demand. Investigations are cited in which it is claimed that alcoholic intoxication is due to acetaldehyde, an intermediate product in the metabolism of both alcohol and paraldehyde. Patients sedated with paraldehyde cease to complain of the symptoms of their physiological disturbances, which may be neglected. Methods of clinical diagnosis of the several physiological disturbances are briefly discussed.

An Experimental Investigation of Sexual Symbolism in Anorexia Nervosa Employing a Subluminal Stimulation Technique.

H. R. BEECH (*Psychom. Med.*, July-August, 1959) has attempted to validate in an objective manner the postulated relationship between ideas concerning food and those concerning sexuality in patients with anorexia nervosa. The technique adopted was that of free association to words which were presented just below the threshold for conscious recognition. The experimental subject was a 27-year-old woman who suffered from anorexia nervosa of long standing, and she evoked significantly more "food" responses to "sex" words than to "neutral" words offered in this word association test. The value of 5·236 for χ^2 confirmed the theoretical prediction at an acceptable level of significance.

Unmarried Mothers.

N. H. GREENBERG, J. G. LOESCH AND M. LAKIN (*Psychosom. Med.*, July-August, 1959) comment on life situations associated with the onset of pregnancy in unmarried mothers. As an incidental finding, while conducting a study on a group of illegitimate children, they noted in some cases a history of separation, significant for the mothers, just prior to the onset of their pregnancies. Conception on occasions had occurred at a rather unusual time of the menstrual cycle. To determine the significance of separation as a determinant of pregnancy, the authors then interviewed 31 unselected unmarried pregnant women, and found that they were particularly sensitive to separations, describing themselves as frequently and severely depressed. Their egos appeared infantile, and interpersonal relationships often showed an anaclitic character. Separation due to recent death of a significant person occurred in at least 13 instances, recent maternal separations were evident in 10 cases, and events considered to be threatened separations or those which can be conceptualized as equivalent to separation (e.g. leaving school, losing a job) were noted. Among many significant events occurring prior to the time of conception in these subjects, the authors noted the phenomena of an object loss with depressive reactions. The pregnancies appeared partly to

represent attempts at reinternalization of an equivalent to the object lost or some substitute. They all denied themselves the use of abortion to terminate the pregnancies, and they did not wish to have the children adopted. The fœtus was rarely seen as an individual-to-be but rather as an object functioning only for the gratification of the mother, suggesting that pregnancy *per se* was more consequential than wished for. In a few cases promiscuity had been present for a period of time without conception taking place, and the authors speculate whether a condition of psychogenic sterility existed until a significant object loss occurred to shift the balance of those forces which had blocked conception.

Manual Perception in Normal Children.

C. MONFRAIX, G. TARDIEU AND C. TARDIEU (*Presse méd.*, April 18, 1959) have studied tactile perception (recognition of objects and geometrical figures) in 218 normal children. They state that the study has enabled them to determine how these gnosias increase as the child develops. In the series, common objects were easily recognized by the age of two and a half years; geometrical figures were not recognized until later. The authors state that the number of geometrical figures recognized increases with age, and this recognition provides a test which makes it possible to determine the "gnosic age" of the child. The test cannot be used before the age of three and a half years, and it permits the differentiation of children aged between three and a half and six years. When the 12 geometrical figures chosen are offered to each hand in succession, the child of four years recognizes the object correctly 10 to 14 times out of a possible 24, the child of five years 14 to 17 times, and the child of six years, 17 to 19 times. The test is not applicable after the age of six years. When used as suggested, it permits the detection of delayed development of gnosia (a term which the authors prefer to astereognosis) in children with motor weakness of cerebral origin. The work is to be continued.

HYGIENE.

Periodic Health Examinations and Multiple Screening.

L. BRESLOW (*Amer. J. publ. Hlth*, September, 1959) discusses the value of periodic health examinations and multiple screening in a preventive medicine programme. The aim of the periodic health examination is to detect disease at a stage where treatment can prevent disability and premature death, and to provide an opportunity for health education and specific preventive action, such as active artificial immunization. It has been applied to specific conditions such as pregnancy, and to various diseases such as cancer, tuberculosis, syphilis and diabetes. The author suggests that the ideal approach to preventive medicine is an annual comprehensive health examination. In pædiatrics more attention is being given to health supervision. Surveys in the U.S.A. have indicated that this is not so for the older age groups. The author suggests that the reason for this is an inadequate number of medical practitioners who are interested in the preventive aspect of medicine. In the meantime, multiple screening is increasingly recognized as a contribution to preventive medicine, as a practical method for the early detection of important diseases and disabilities. Mass multiple screening is the application of tests rapidly and economically to large groups of apparently well persons, to identify those individuals in the population who probably have abnormal conditions. Such persons are then referred for confirmatory diagnosis and treatment if needed. The results of a number of screenings are given. In one such screening, the tests used were: measurement of height, weight and blood pressure; blood tests for diabetes, syphilis and anæmia; a urine test for albumin; and vision tests. More than half those tested had significant findings and were referred to their own physicians. The author recommends further research to improve the specificity and sensitivity of the tests used, to reduce their cost, to develop new tests and to determine the tests and examination procedures most suitable for various segments of the population.

The Luoto Capillary Agglutination Milk Test and Bovine "Q" Fever.

R. A. TJALMA AND J. L. BRAUN (*Amer. J. publ. Hlth*, August, 1959) investigated the Luoto capillary agglutination milk test as a method of identifying and documenting bovine "Q" fever infection. In addition, the testing of bulk or pooled milk for evidence of herd infections was investigated. It was found to be a reliable and valid method of identifying "Q" fever infections in dairy herds and cows. The validity of the test was demonstrated by the correlation of milk and blood "Q" fever titres of individual animals and the isolation of "Q" fever organisms from samples of infected milk. During the investigation it was found that serologically positive cows had one or more udder quarters that were producing infected milk while milk from the remaining udder quarters was uninfected. The authors suggest that this indicates that the site of localization of "Q" fever is in the affected udder quarter, and that it is necessary to collect a complete milk sample from each quarter before testing for "Q" fever by the capillary agglutination method.

Antibodies against Enteric Pathogens in Human Gamma Globulin.

E. NETER *et alii* (*Amer. J. Publ. Hlth*, August, 1959) investigated the presence of enterobacterial antibodies in human gamma globulin by agglutination and hæmagglutination methods. The organisms concerned included salmonellas, shigellas and enteropathogenic *Escherichia coli*. Complete antibodies against these organisms were detected by the hæmagglutination test in titres exceeding those obtained by the conventional bacterial agglutination method. Incomplete antibodies were demonstrated by the antiglobulin hæmagglutination and enzyme hæmagglutination procedure, and the titres were up to sixteen-fold higher than those obtained by the hæmagglutination method. Similar titres of these antibodies were found in gamma-globulin preparations obtained from the U.S.A., Japan, India, England and Australia, except that complete antibodies against *S. paratyphosa* A and *S. dysenteriæ* Type I were found in preparations from India, but not from the U.S.A. and Japan. Absorption tests confirmed the specificity of the hæmagglutination method. The possible implications of the findings, with particular reference to the clinical use of human gamma globulin, are discussed.

The Effect of Prematurity on Health and Growth.

H. KNOBLOCH *et alii* (*Amer. J. publ. Hlth, September*, 1959) have compared the incidence of illness and physical defect and subsequent growth patterns in relation to weight at birth in a group of 500 premature and 492 full-term control infants, comparable in respect to various socio-economic variables. The findings agree with those of other investigations, and indicate that at 40 weeks of age the premature infants, in comparison with full-term control infants, are from 0·5 to 1·0 inch shorter and from 500 to 1000 grammes lighter, have two to three times as many physical defects, and have 50% more illness. When the presence of serious neurological abnormality resulting from cerebral damage is taken into account, the physical disadvantage of the premature infants is even more marked. The findings suggest that those factors responsible for producing the increased cerebral damage in premature infants have a generalized deleterious effect as well, and lend additional support to the necessity for preventing prematurity in order to effect substantial reductions in the incidence of physical and neuropsychiatric disability.

Toxicological Studies of DDVP in Tobacco Warehouses

W. DURHAM, W. HAYES AND A. MATTSON (*A.M.A. Arch. industr. Hlth*, September, 1959) have carried out tests in tobacco warehouses to determine the toxicity of DDVP (0,0-dimethyl 2,2-dichlorovinyl phosphate) to mammals and its effectiveness against the cigarette beetle. In some tests, DDVP was dissolved in perchlorethylene and sprinkled on the floors; in other tests it was applied as a thermal aerosol. Dosage levels studied were 0·5, 1·0, 2·0 and 10 mg. per cubic foot. Human volunteers spent up to eight hours per day and rats and monkeys were confined continuously in the treated warehouses. Concomitant studies of concentration of DDVP in the air were made. No signs or symptoms of DDVP intoxication were noted in volunteers or experimental animals. All species showed some degree of cholinesterase depletion after exposure to the highest DDVP application. Aerosol application of DDVP produced less cholinesterase effect than did sprinkling of a perchlorethylene solution of DDVP. The authors concluded that DDVP would be safe for warehouse workers when applied twice a week, or less often, at a rate of 2 mg. or less per cubic foot as a thermal aerosol.

Special Article.

DOCTORS WITHOUT CREDENTIALS IN AUSTRALIA.[1]

ALTHOUGH Australia is a single nation, it is essentially a federation of six States, each with sovereign powers. The Federal Government possesses only those powers surrendered to it by the States, and the control of the right to practise medicine is not one of them. Each of the six States and the Australian Capital Territory has its own relevant legislation, which is administered by a medical board, and registration requirements vary from one to another.

New South Wales.

An overseas doctor who applies to be allowed to practise medicine in New South Wales must prove that he has studied for five or more years in a school of medicine in a foreign country, and, after proper examination, has received a degree or diploma certifying to his ability to practise medicine or surgery in such country. A series of further provisions, related to the particular candidate's qualifications, then allow for registration forthwith in special cases, after a period spent in practice under supervision or in certain designated regions, or after completing and passing the examinations in the concluding years of the medical course in the University of Sydney. With regard to proof of basic qualifications, the Medical Board accepts for record purposes photostat copies of documents, particularly if the original is available for comparison with the copy. In other cases, wherever possible, certified photostat copies are accepted in lieu of originals which may not be available for comparison. When neither the original nor certified photostat copies of documents are submitted, photostat copies, if accompanied by other relevant documentary evidence which supports the authenticity and *bona fides* of the photostat copy, have been accepted. As the law stands, an application without documents (even though the applicant could credibly be believed to have lost them from any cause) could not be considered.

Victoria.

In Victoria, registration is normally granted to those who have received a degree or diploma certifying to their ability to practise medicine or surgery from recognized medical schools or universities in most countries of the British Commonwealth. For those who hold a medical degree or diploma of some other country, registration is granted forthwith in special cases, but usually only after completion of a further period of study and the passing of the necessary examinations in the medical school of an Australian university. The normal requirement for applicants for registration is that they produce the originals of degree certificates by virtue of which they seek registration. In special cases, however, the Medical Board may accept photostat or other copies of certificates, provided that they are correctly certified as true copies by some medical person or authority recognized by the Board. Before a copy is recognized, an applicant must submit a statutory declaration to the effect that the original certificate cannot be produced. All applications for registration, whether supported by original certificates or copies, are considered individually by the Board, and all applicants must produce indisputable evidence of their identity.

South Australia.

It is the policy of the Medical Board in South Australia, with regard to the registration of overseas qualifications, to recognize only those whose qualifications are approved of and registrable by the General Medical Council of Great Britain. The Board will accept photostat copies of qualifications provided that the identities of the persons presenting them are definitely established as the persons named in them. In the absence of the original copy or a photostat copy of the qualifications, the board would accept an official certificate forwarded direct from the body granting the qualifications.

Queensland.

In Queensland, registration is granted to holders of a degree, diploma or certificate in medicine or surgery of any university, college or any other body in Great Britain, Northern Ireland, the Commonwealth of Australia, or the Dominion of New Zealand, subject to certain qualifications relating to hospital experience. Holders of medical qualifications of a suitable standard from other countries may be granted full or limited registration after passing an examination conducted by the medieal professors in the University of Queensland. Applicants are required to produce their degree certificates or evidence satisfactory to the Board when the degree certificates themselves cannot be produced. The acceptance of photostat copies of degree certificates and other documents is a matter for consideration by the Medical Board in each individual case. Photostat copies which have been certified by an authority such as a notary public to be true copies of the original would probably be acceptable, but mere photostat copies without certification would be open to question.

Western Australia.

Registration in Western Australia is now normally granted to those with degrees from universities in Australia and New Zealand, and to those registrable in Great Britain under what is generally known as the Home List, subject to certain qualifications of experience, good character and identification. Applicants who satisfy the Board in all respects but are unable to produce documentary evidence of their qualifications are required to complete a suitably worded statutory declaration and to produce a certificate from the university or college concerned to the effect that such qualifications have been granted. Photostat and similar forms of copies are acceptable provided that they are certified by a qualified witness as copies of the originals.

Tasmania.

Registration in Tasmania is granted only to applicants who are registrable by the General Medical Council of Great Britain. Generally speaking, production of the original diploma is required, but on occasions a special certificate has been accepted from the university from which the applicant claims that he has graduated. Photostat or other forms of credentials would be accepted only if there was ample supporting evidence. Special provision is made in the Tasmanian legislation for training of foreign doctors not immediately registrable, and in such cases a sympathetic attitude has been adopted at times when candidates have had very real evidence to support their claim of qualification. However, such doctors are required to undergo a period of hospital training and to pass a qualifying examination before they can be registered.

Australian Capital Territory.

In the Australian Capital Territory registration is granted only to medical practitioners from overseas who can prove to the satisfaction of the Registration Board that they have passed through a five-year regular course in medicine and surgery in a part of the Queen's Dominion, namely the United Kingdom, and that they hold a qualification which has allowed them to be registered under the Medical Acts of the Parliament of the United Kingdom. The Registration Board requires that the applicant produce his original degree. Photostat copies of documents are not acceptable for registration, but photostat copies of originals are kept for record purposes only. A medical practitioner who has lost his documents through war, fire or similar causes would have to obtain copies or evidence of the like to place before the Registration Board for consideration, such as a certificate from the university at which the qualifications were obtained. The final decision would be at the discretion of the Board.

RONALD R. WINTON.

[1] One of a group of articles from various countries contributed by request and originally published in the *World Medical Journal*, March, 1959. It is reprinted here by permission.

British Medical Association.

SOUTH AUSTRALIAN BRANCH: SCIENTIFIC.

A MEETING of the South Australian Branch of the British Medical Association was held at the Repatriation General Hospital, Springbank, South Australia, on October 30, 1958, the President, DR. C. C. JUNGFER, in the chair. The meeting took the form of a series of clinical, pathological and radiological demonstrations by members of the medical, surgical, pathological and radiological staffs of the hospital.[1]

[1] Acknowledgement is made to the Chairman of the Repatriation Commission for permission to publish details concerning patients under the care of the department.

Empyema with Unusual Features.

DR. W. J. R. WYNESS presented details of the case of a man, aged 47 years, who had been admitted to hospital in December, 1957, with a diagnosis of pleurisy with effusion, thought possibly to be tuberculosis. Three months previously the patient had become ill. At that time he suffered from coughing and a constant ache in the right chest posteriorly. He remained "off colour" for six weeks, at about which time he became short of breath and suffered a sharp pain in the right chest. He was now coughing more frequently, the cough producing purulent sputum. He sweated and became febrile. Therapy with penicillin improved him, but he did not become well. His cough worsened, and he became severely ill with increased pain in the chest, and increased sputum, which was now rusty in colour. An X-ray film of the chest on November 23 had shown slight opacity laterally in the right mid-zone, probably in the posterior segment of the right upper lobe. A further film on December 1 showed a large right pleural effusion. Straw-coloured fluid was aspirated on the same day (28 ounces), and a further 24 ounces on the following day.

On admission to hospital, clinical and radiological examination of the patient showed a large right pleural effusion, and a further 31 ounces of straw-coloured fluid were aspirated. The fluid was sterile on microscopic examination and culture, containing some erythrocytes and numerous polymorphs. His fever increased to 102° F., and a leucocytosis developed, of 12,400 cells per cubic millimetre, 83% of those being polymorphs. He was treated with "Terramycin" and "Chlormycetin", without clinical response. By December 18 it was thought that his effusion was probably tuberculous, and streptomycin and iso-nicotinic acid hydrazide therapy was instituted. A bronchoscopic examination on January 7, 1958, showed only a crowding of the right lower lobe bronchi. His symptoms did not improve. Cough, purulent sputum and pain were prominent features. On January 13 further fluid was aspirated from the right chest, and was still straw coloured. His cough produced some purulent sputum. On January 23 a chest aspiration produced two cubic centimetres of thick creamy pus, which contained a few *Streptococcus viridans* at bacteriological examination.

Dr. Wyness stated that it was considered that the diagnosis was one of loculated empyema which had ruptured into the lung. Decortication was considered the treatment of choice, and on January 30 that operation was performed, a right posterior segmental resection being done for lung abscess, as well as the right pulmonary decortication. The pathological features of the specimen removed were a thickened empyema wall with the histological features of a walled-off abscess, and the lung showed the classical features of severe organizing pneumonia. After the operation his recovery was uneventful.

Dr. Wyness stated that the lesson to be learned was that empyema was not always easy to diagnose, and in the case under discussion considerable difficulty had been experienced.

Staphylococcal Pneumonia with Spinal Complications.

Dr. Wyness's second case was that of a man, aged 62 years, who had been admitted to hospital on January 6, 1958. In October, 1957, he had suffered from severe staphylococcal pneumonia complicated by nephritis. That illness had responded slowly to "Synermycin" therapy. He had been discharged from another hospital early in December, 1957, with a draining sinus, the result of an abscess in the right buttock which had been incised. A further fortnight's in-patient therapy then proved necessary in the same hospital for severe back pain thought probably to have been due to a perinephric collection, which then responded to chloramphenicol therapy.

On admission to hospital, he was found to have a marked rigidity of the lumbar spine, with increased lordosis, and scoliosis concave to the left. The left mid-lumbar region was tender, and the left leg was "held awkwardly". Anæmia was present, the hæmoglobin estimation being 9·6 grammes per 100 millilitres, and a leucocytosis of 10,500 cells per cubic millimetre was present, of which 68% were polymorphs. The erythrocyte sedimentation rate (Wintrobe) was 60 millimetres in one hour, and microscopic examination of the urine showed a few erythrocytes, leucocytes and hyaline casts, but the urine proved sterile on culture. Intravenous pyelography showed no renal or other urinary abnormality. The scoliosis was also observed from the X-ray film, and the disk space between the second and third lumbar vertebræ was narrowed on the left side.

The patient's pyrexia persisted during February. His anæmia was treated by a transfusion of two pints of blood. However, his pain continued. Sternal marrow examination gave normal findings, lupus erythematosus cells being absent from the normal fatty marrow. On February 18 the patient's pain became much worse, and he complained of pins and needles in the buttocks, worsened by coughing. A lumbar puncture on February 24 at the level of the third to fourth lumbar vertebræ showed a low pressure and an abnormal result to the Queckenstedt test. The cerebro-spinal fluid was clear, with 35 erythrocytes per cubic millimetre, 30 leucocytes (mainly lymphocytes) per cubic millimetre, and a protein content of 1500 milligrammes per 100 millilitres. The lumbar puncture was repeated at the level of the first to second lumbar vertebræ two days later. The Queckenstedt test test there showed a normal response. The cerebro-spinal pressure was 160 millimetres of fluid. The fluid contained 500 erythrocytes and 40 leucocytes per cubic millimetre, with a protein content of 160 milligrammes per 100 millilitres. The following day the ankle jerks were reduced, and the patient complained of pains going into the legs. Neurological opinion was that there was a space-occupying lesion of the cauda equina or conus medullaris either neoplastic or inflammatory in origin.

The X-ray examination of the lumbar spine on the same day showed a partial destruction of the upper left side of the third lumbar vertebra, typical of osteomyelitis. The patient was seen in consultation by the neurosurgeon (Mr. L. C. E. Lindon), who concluded that signs were present of an acute pachymeningitis externa or extradural abscess, with disk involvement at the level of the second to third lumbar vertebræ. Exploratory laminectomy was performed on March 10. After removal of the spinous processes of the second and third lumbar vertebræ, it was found that the left side of the disk between the second and third lumbar vertebræ was the site of inflammatory infiltration. The left (second to third lumbar vertebræ) apophyseal joint was disorganized. The third lumbar nerve root was involved in the inflammatory lesion. The material removed by the neurosurgeon was described as amorphous on histological study by the pathologist, and was found to be sterile on culture.

Subsequent treatment was by immobilization in a plaster shell and treatment with various antibiotics. The draining wound subsequently became infected by coagulase-positive staphylococci. The patient became pyrexial again in May, and X-ray examination showed an area of destruction in the second lumbar vertebræ. A sinugram outlined a cavity behind the laminæ. The cavity was then incised and packed. The patient was at the time of the meeting (October), much better, but a discharging sinus was still present.

DR. R. G. MCEWIN asked on what grounds the diagnosis of staphylococcal pneumonia had been made.

DR. R. A. BURSTON, to whom Dr. Wyness referred the question, stated that the diagnosis was made on the clinical features, as well as on the recovery of staphylococci in the sputum. He (Dr. Burston) had been the attending physician at the time. A severe complication with that illness had been the patient's becoming anuric. The blood urea nitrogen level rose to 440 milligrammes per 100 millilitres, after which the patient recovered.

Multiple Renal Tumours and Bowel Carcinomata.

Dr. Wyness next presented details of the case of a man aged 71 years. He had been admitted to hospital on July 16, 1958, with a four-day history of passing bright red blood in his urine, which was painless. A similar attack had occurred a year previously. He was investigated by intravenous pyelography, which revealed a defect in the left major cephalic calyx.

A left nephrectomy was performed on August 21. That revealed two lesions: (i) a papillary tumour of the renal pelvis; (ii) a papillary type of cortical adenoma.

An interesting feature in his previous history was that he had had three adenocarcinomata, apparently not recurrences, removed from the colon: (i) from the sigmoid colon in 1944; (ii) from the sigmoid colon in 1952; (iii) from the junction of the caecum and the ascending colon in 1956.

DR. C. W. KINGSTON discussed the pathological features of the case, and illustrated his talk with projected colour slides. The first of those were photomicrographs of the segment of bowel removed in 1952. They showed the conjunction of normal and cancerous epithelium. The tumour was an adenocarcinoma of the columnar epithelium, and the typical features of the adenocarcinoma were shown in the photomicrographs—the bizarre pattern of cells, the mucoid secretion, hyperchromatism of the nuclei and numerous mitoses. Other photomicrographs showed a

grade II papillary carcinoma of the renal pelvis (1958 specimen). That showed a papillary structure, with several layers of transitional epithelium present in a disorderly pattern with numerous mitoses. Dr. Kingston stated that in the gross specimen submitted, a second tumour of the medulla lay alongside the tumour just described, and was thought to be an infiltration from it. However, sections (demonstrated in photomicrographs) showed a cortical adenoma of the common papillary pattern, situated on the renal medulla. The second mass was a papillary tumour of tubule epithelium, and obviously distinct from the other two tumours recorded. Its medulla location was unusual. The tumour was a small one, with well differentiated structure, and showed no evidence of invasion. Histologically, however, it was difficult to make pronouncements about invasion, since benign-looking tumours often metastasized. Dr. Kingston concluded that in the case under discussion there were at least two malignant tumours of obviously different tissues. It was interesting to note in passing that multiple malignant disease was not uncommon to the pathologist, though less commonly diagnosed in clinical practice. Warren and Gates (quoted in Anderson's text-book of pathology) stated that there was a tendency amongst cancer patients for multiple cancers to develop, which was six times the normal expectation.

DR. R. HUNTER asked if Dr. Wyness's case was thought suitable for total colectomy, and asked how much of the colon had been left by the surgeon.

DR. A. F. HOBBS, in reply, stated that a good part of the transverse and descending colon, as well as of the sigmoid colon, had been left at the operation. At operation no polypi had been detected. Total colectomy had been considered at the operation, but it was thought that the giving of a permanent ileostomy to the patient was not warranted in that case.

Dr. W. J. R. Wyness commented that the patient had suffered from chronic bronchitis and myocarditis since 1948.

DR. T. P. DEARLOVE referred to Wangensteen's experience over 10 to 15 years with malignant diseases and polypi of the large bowel. Wangensteen had found the recurrence rate rather high, and he had perhaps hinted that total colectomy might have been of value. Dr. Dearlove continued to say that, whilst many of those present would feel dubious about accepting any such radical regime, it was obvious that the views of a person with such vast experience as Wangensteen had had, were well worthy of consideration.

Dr. A. F. Hobbs referred to overseas experience, which had shown that in cases in which operation had been performed for carcinoma of the colon, and in which further polypi had been discovered, in only 2% of cases was there a development of further carcinoma. He was, therefore, emphatic that in the case under discussion a total colectomy was not indicated.

Two Cases of Carcinoid Tumour.

DR. D. S. FORBES presented details of two cases of patients suffering from metastasizing carcinoid tumour. In one case the appendix was the seat of the tumour, and in the other the ileum.

The first case was of a National Service trainee aged 20 years, who presented with a 24-hour history of right-sided lower abdominal pain and vomiting. On examination, the temperature was 99·2° F., and the pulse rate was 88 per minute. There was acute tenderness with guarding in the right iliac fossa. At appendicectomy a gangrenous appendix was found with a moderate amount of mucopurulent peritoneal fluid. The post-operative course was uncomplicated.

The macroscopic pathological report of the specimen was as follows: "The specimen consists of a curved appendix measuring 8·0 centimetres long and 1·8 centimetres in maximum diameter. The appendix was constricted 1·0 centimetre from its tip. Distal to the constriction the tip of the appendix was filled with yellow tumour about 0·5 centimetre diameter. At its centre the growth appeared to infiltrate to the meso-appendix, and a small yellow nodule of growth was found in the adjacent portion of the meso-appendix. The line of excision appears to be clear of the visible portions of the tumour. The proximal portion was very swollen and its lumen distended, and contained several large fæcoliths. The whole of the peritoneal surface was injected." Dr. Forbes stated that Dr. Kingston would discuss the histological features seen. The significant finding was that microscopic infiltration by carcinoid material was found in the regional lymphatics. In view of that finding, it was decided to perform a right hemicolectomy, and it was performed six weeks after the appendicectomy. Three inches of ileum, the ascending colon, and three inches of transverse colon with glands proximally as far as the origin of the ileo-colic vessels were removed. The specimen showed no macroscopic evidence of carcinoid material. However, microscopic examination of 14 lymph nodes showed carcinoid tumour in one node lying along the ileo-colic artery (discussed further by Dr. Kingston).

The second case presented by Dr. Forbes concerned a male, aged 67 years, who presented with a six weeks' history of severe intermittent central abdominal pain. The pain was more noticeable one quarter to one half an hour after meals, and occasionally wakened him at night. There was no vomiting, flatulence or other disturbance in bowel function. His weight was constant at nine stone four pounds. During the ensuing two weeks, the intensity of the lower abdominal pain increased and he developed diarrhœa. His local medical officer recorded tenderness and rigidity in the hypogastrium. His symptoms were thought possibly to be due to a bowel infection. On further interrogation, the patient admitted to having had bouts of intermittent colicky lower abdominal pain for several years. He also admitted having had morning vomiting for three months prior to his admission to hospital.

Examination of the abdomen was difficult, because of the patient's inability to relax. However, there was the suggestion of a mass in the right lower abdomen. Rectal examination revealed no abnormality. Investigation of the blood, urine and fæces and an X-ray examination of the bowel with a barium enema revealed no abnormality. The Wassermann and Kline reactions were negative. X-ray examination with a barium meal and follow-through showed the small bowel pattern to have an unusual distribution, which suggested that the small bowel was displaced by a rounded mass. Intravenous pyelography showed a small diverticulum on the right side of the bladder; that was confirmed at cystoscopy. There was no other abnormality of the renal tract. Examination of the abdomen under general anæsthesia revealed a firm tumour four inches in diameter just below the umbilicus and a little to the right of the midline. The mass was not attached to the anterior abdominal wall, and was freely mobile in all directions.

At laparotomy, a greyish-white segment of ileum about seven inches long was found three feet from the ileo-caecal valve. The segment was of rubbery consistency, and was rigid. The bowel immediately above the affected segment was slightly distended, hypertrophied and purplish in colour. The segment below the affected segment was similar in colour, but not distended or hypertrophied. In the mesentery, which was shortened to nil, there was a mass, which was continuous with a larger mass retroperitoneally. An opening was made into it immediately above the affected bowel, and about six ounces of creamy pus, with a slight *Escherichia coli* odour, were evacuated. Subsequent culture revealed a mixed growth of *E. coli*, *Streptococcus fæcalis* and an atypical *Alcaligenes fæcalis*.

It was thought at the time of operation that the findings recorded were consistent with a diagnosis of regional ileitis. In view of the acute nature of the process and the fact that no definite obstruction was demonstrated, no bowel resection was performed. The abscess cavity was drained, and the abdomen closed. Apart from a slight chest infection, his post-operative course was uneventful; the patient lost his abdominal pain, and his bowel function returned to normal over a period of four weeks.

He was readmitted to hospital one week after discharge with symptoms and signs of small bowel obstruction. It responded to drip and suction. However, during the ensuing week, he continued to have intermittent small bowel obstruction. The decision was made to explore the abdomen again with a view to resecting the offending segment of ileum.

At the second operation, the same area of greyish-white ileum, previously described, was present. The bowel, for three feet above the affected segment, was discoloured and dilated, and the attached mesentery thickened and œdematous. The small bowel mesentery other than that attached to the affected loop of bowel showed scattered, small, raised, white plaques about two millimetres in diameter. Approximately four feet of affected ileum were resected, and continuity was restored with the use of an end-to-end anastomosis. The patient made a rapid recovery from the operation, and was discharged from hospital three weeks later, his bowel functioning normally.

The pathologist's report of the specimen stated: "Macroscopically the distal portion of the specimen was thickened,

its mesentery puckered and shortened, the bowel coiled together in a bunched mass. On section, numerous submucous yellow nodules were found. There was considerable fibrosis of the mesentery, containing a number of scattered yellw nodules. Several of the lymph nodes were infiltrated with yellow tumour." The microscopic study, which revealed a carcinoid tumour, would be discussed further by Dr. Kingston. The diagnosis was, therefore, one of a metastasizing carcinoid tumour of the ileum.

He was reviewed three months after the operation. During that period he had remained symptom free and had gained 21 pounds in weight.

Dr. C. W. Kingston discussed the pathological aspects of the cases of carcinoid tumour, illustrating his talks by coloured photomicrographs. He referred first to the case of carcinoid of the appendix, and showed the general pattern of cells under the low power, showing solid cell clumps of varying size, filling the lumen of the appendix, infiltrating the muscle layer, and spreading out to the meso-appendix and under the serosa. Under the high power, he showed details of cell structure stained with hæmatoxylin and eosin; uniform rounded nuclei and finely granular eosinophilic cytoplasm with poorly defined cell boundaries were present. With argentaffin stain, those cells were particularly prominent, with numerous coarse black granules in the cytoplasm. The high power also showed that there was infiltration of lymphatics of the meso-appendix. Sections of the affected lymph node showed several small tumour emboli in the peripheral sinus, and one larger deposit infiltrating along a trabeculum. High power showed the characteristic cell appearance of the original growth, and the striking argentaffin reaction.

Dr. Kingston stated that although appendiceal carcinoid tumours were comparatively common, metastasis from them was rare. The opposite obtained for carcinoid tumours of other parts of the intestinal tract. Two recent articles had surveyed the world literature of the subject of malignant appendiceal carcinoid tumours, and had come to very different conclusions. Knowles *et alii* (*Journal of Pathology and Bacteriology*, 1956, 72: 326) reviewed a series of 129 cases drawn from the literature, and concluded that in 60% muscle was infiltrated, and in 50% the tumour reached the serosa. Nevertheless, they considered that only 15 acceptable cases of metastasis from appendiceal carcinoid tumours were reported in the whole of the literature. Their criterion of infiltration was that of macroscopic infiltration of lymph channels, or macroscopic evidence of metastasis in the lymph nodes.

On the other hand, MacDonald also reviewed the literature as well as 207 further cases drawn from Boston hospitals (*American Journal of Medicine*, 1956, 21: 867). Of the latter group, only about 6% invaded muscle, 5% were subserosal, only 1% had spread to local lymph nodes, and none showed distant metastases.

Both of these articles considered that most of the so-called malignant cases recorded in the medical literature were so poorly documented as to make their designation as malignant unacceptable. MacDonald defined as malignant those cases in which were present infiltrated muscle coats, serosa, lymphatics or blood vessels, and in which extra-appendiceal origin had been excluded. Using those criteria, he accepted only 13 cases of malignant disease that had been recorded. Of these, in two cases there was spread to regional lymph nodes, and in none was there distant metastases. Knowles *et alii* recommended hemicolectomy when lymphatic involvement of the appendix was identified, but otherwise preferred simple appendicectomy. MacDonald recommended local removal of the appendix and dissection of the local lymph nodes if involved. Dr. Kingston stated that the case presented indicated that the recommendation of MacDonald was inadequate, as a distant lymph node had shown microscopic evidence of metastasis, and that the recommendation of Knowles *et alii* was to be preferred in those rare cases. Hemicolectomy was performed in the first case, and subsequently the urine test showed normal quantities of 5-hydroxyindole acetic acid.

Dr. Kingston referred then to the pathological features of Dr. Forbes' second case, one of ileal carcinoid tumour. The specimen removed at operation was shown, which demonstrated a typical small bowel case of carcinoid tumour of multicentric origin. Slides of the histological features of the specimen were shown also. Those demonstrated, by hæmatoxylin-eosin and argentaffin staining, a growth similar to that of Dr. Forbes' first case, but with some additional characteristic features. Those were the presence of oval cells in clumps, closely applied to one another, and the tendency to form rosettes, as well as peripheral palisading of the cells. Dr. Kingston stated that sections of the mesentery, the lymph nodes involved and other parts of the bowel had all shown similar histological features.

Dr. Kingston stated that carcinoid tumours secreted serotonin, which was metabolized in the lungs to 5-hydroxyindole acetic acid. The latter could be tested in the urine by a simple laboratory investigation. He pointed out that it should be remembered that the secretion of serotonin was erratic, and the test might, therefore, need to be repeated. Dr. Forbes' second case did not show the carcinoid syndrome due to serotonin — of flushing, cyanosis, and diarrhœa, even though after operation he was found to have an excess of 5-hydroxyindole acetic acid in the urine. It was presumed, therefore, that he was able to break down the full amount of serotonin formed. It should be noted that the carcinoid syndrome to date had been reported only in the presence of large secondary carcinoid metastases in the liver. In that case, the liver had been palpated at operation and was apparently free from secondary carcinoid metastases.

Dr. Hobbs stated that he would like to emphasize certain points of practical importance. The first of those was that carcinoid tumour of the appendix was not particularly uncommon. Possibly the frequency observed was due largely to the frequency of appendicectomy. He stated that 99·5% of cases of carcinoid tumour of the appendix were cured by appendicectomy. The other 0·5% showed a lymphatic spread at histological study, and those should be treated by a removal of the right colon down to the ileo-colic artery. Carcinoid tumour of the ileum was most commonly found at post-mortem examination. However, in the last twelve months, he had treated two local cases of carcinoid of the ileum. In one case the tumour had been found six inches from the ileo-caecal junction at appendicectomy by a country surgeon, with lymph gland spread found at histological study. A right colectomy was performed subsequently by Dr. Hobbs, and metastases were found in the regional lymph glands.

Dr. Hobbs considered that the indications for surgery in cases of carcinoid tumour were moderately clear. The tumour was a slow growing one, and it might take a number of years for metastases to develop. Cases had been reported of successful removal of metastases in the liver. He regarded the urinary serotonin test as most valuable as a lead as to whether there were residual metastases present after operation. He suggested that operated cases should be followed up by that test at twelve-monthly intervals. The cases discussed illustrated that every appendix should be opened after operation and a search made for the tumour. Dr. Hobbs stated that he had seen about a dozen cases of appendiceal carcinoid tumour over the years.

DR. R. HECKER referred to a case he had seen privately. He had been called to see a man in consultation in the middle of the night. Over about two hours the blood pressure had fluctuated between 40/20 and 90/50 millimetres of mercury. The following day the X-ray examination of the chest and the electrocardiogram gave normal findings. No obvious cause for the circulatory collapse was found. There was no evidence of myocardial infarction or pulmonary embolism. There had been a history of a removal of a carcinoid tumour of the caecum six months before. Since then recurrent diarrhœa had occurred. Further abdominal surgery had not yet been performed, but a slight excess of 5-hydroxyindole acetic acid indicated probable metastases. Dr. Hecker stated that recurrent vascular collapse was a well-known method of presentation of carcinoid tumour.

DR. H. R. GILMORE referred to a female patient he had seen in consultation suffering from vascular collapse, but without erythema or cyanosis. Subsequently, there was an illness lasting eighteen months, during which a systolic murmur was present, suggestive of a lesion in the right ventricular outflow tract. Shortly before death, which occurred after an 18 months' course, the more typical picture of alternating erythema and cyanosis appeared. At autopsy, performed in conjunction with Dr. H. Lander, a carcinoid tumour of the appendix with limited liver metastases had been discovered. At no stage had there been any symptoms referable to the gastro-intestinal tract.

Pulmonary Tuberculosis.

DR. K. MUGFORD presented details of a case of pulmonary tuberculosis in a man aged 36 years. On admission to hospital, the patient had given a history that for about the last seven years he had had a cough, productive of sputum,

the colour of which had usually been whitish or brownish, and which he thought was due to heavy smoking (more than 30 cigarettes per day). Also during that time he found he was becoming more tired after each day's work as a builder. His appetite had been good except after his occasional drinking bouts, and his weight had been constant at about nine stone seven pounds. He had not noticed night sweating, except during the summer months, which was not considered significant. He found he was becoming more short of breath on exertion. One month prior to his admission to hospital he had had two frank hæmoptyses. There was no history of previous illnesses, and he stated that he had enjoyed excellent health. His father had died of pulmonary tuberculosis 30 years earlier.

Clinical examination was non-revealing, except for an area of crepitations at the right apex posteriorly. The Mantoux test gave a positive result at a 1/1000 dilution. Examination of a direct sputum smear revealed numerous acid-fast and alcohol-fast bacilli, morphologically resembling *Mycobacterium tuberculosis*, and culture showed acid-fast and alcohol-fast bacilli culturally resembling *M. tuberculosis*. An X-ray examination of the chest revealed an abnormal mottled shadowing in the upper and mid zones of the right lung. The shadowing was very heavy in the right apex lobe, where shadows indicating fibrous strands radiating to the hilum were seen. The radiologist suggested the presence of cavitation in the right upper zone. Tomographic examination confirmed the presence of right upper zone cavitation and heavy upper lobe disease. The apex of the lower lobe appeared clear on the tomogram.

A full course of streptomycin, one gramme daily, isonicotinic acid hydrazide, 300 milligrammes daily, and para-amino salicylic acid, 12 grammes daily, was instituted. After three months of medical treatment, his sputum was still positive for acid-fast bacilli. That was considered to indicate that the cavity of the right apex was still present, although the X-ray film of the chest showed clearing of the lesion. He was therefore recommended for surgical treatment after another month of antituberculosis therapy.

At operation, a right upper lobectomy and apical segmental resection of the right lower lobe were performed with compensatory thoracoplasty. The right upper lobe was found to be extensively diseased. In addition, the apical segment of the right lower lobe was studded with pea-sized tubercles. Apart from a small indurated collection along the medial border of the right middle lobe, the remainder of the lung felt normal to the surgeon. Histological study of the resected lung demonstrated obscure tubercles, but no tubercle bacilli.

Dr. Mugford stated that the case was presented as a fairly typical case of pulmonary tuberculosis. The period from diagnosis until the patient's discharge from hospital was about seven months. That period included four months of medical treatment, followed by surgery and continuity of medical treatment for a further period of three months. He expected that the patient would be back at work within a total period of about 12 months. Dr. Mugford concluded that the case was presented to demonstrate what could be done for a patient with fairly extensive bilateral pulmonary tuberculosis.

Chronic Bulbar Palsy.

DR. R. V. SOUTHCOTT presented details of the case of a patient with chronic bulbar palsy from motor neurone degeneration. The history of the patient was as follows: in 1949, at the age of 53 years, he had first noticed that there was something wrong with his speech, and that he felt "run down". His weakness had progressed, and he had to give up work. There had been a fairly rapid deterioration over the next year or so, but he had not been admitted to hospital until 1954. By then he was experiencing considerable difficulty in swallowing, and was practically completely anarthric. Spastic tetraplegia was present, which had been in evidence for six months or longer. There was also wasting of the intrinsic muscles of the hands. A diagnosis was made of motor neurone degeneration affecting mainly the brain stem. His condition at the time of the meeting had not altered much from what it had been in 1953 or 1954. He was now 62 years of age, and had had the disease for nine years, of which the last four years had been spent in hospital. Glosso-labio-laryngeal paralysis was present with fibrillary movement of the lips and tongue. The tongue could be moved forwards at the most about a quarter of an inch. Wasting of the shoulder musculature and of the intrinsic hand musculature were still present, and also spastic tetraplegia. The intellect remained unimpaired. He still had a keen sense of humour, and had always been cheerful and likeable, despite the severity of his disease. There was no disorder of sensation. As the patient was unable to speak, it was necessary at a neurological examination to get the patient to give a sign to distinguish, for example, a sharp point from a blunt one, along the lines of Dumas in "The Count of Monte Cristo". The patient could move his thumb quite well, and the thumb was waggled for "yes" when the presence of sensation was required, or when discrimination was required then twice for "sharp" and once for "blunt" and so on. In summary, therefore, there was an incomplete progressive motor neurone disease with bulbar and cervical involvement, as well as cortico-spinal tract degeneration with little progression over the last four years.

Dr. Southcott discussed the differential diagnosis of those conditions. That was considered to represent little problem here. He believed chronic motor neurone disease was best regarded as one entity, with many facets. Lower motor neurone degeneration resulted in progressive muscular atrophy. Amyotrophic lateral sclerosis included spinal atrophy with cortico-spinal degeneration (including the Betz cells) with cortico-spinal tract degeneration. The best surveys of the condition (here reference was made to the work of Swank and Putnam) indicated that all the various diseases grouped under the heading of motor neurone degeneration merged insensibly into one another. In some cases of bulbar palsy, heredo-familial factors could be found, for example in Friedreich's ataxia, but no such factor was found in general in motor neurone degeneration, and although toxic factors might be suspected, none had been definitely incriminated. Fortunately, the disease was a rare one.

The case was demonstrated from the point of view of clinical interest in an unusual condition, but more particularly from the point of view of management of a chronic illness. Such patients had difficulty in coughing and sneezing and, therefore, suffered risks from the inhalation of food and secretions. The patient demonstrated retained some power of coughing, which resulted in a hoarse bellow. Up to the time of the meeting no major respiratory complication had occurred. As expected, urinary difficulties occurred. He became unable to void urine two and a half years earlier, and had recurrent partial bladder paralysis with retention of urine. That was thought to be entirely of neurological origin as no prostatomegaly had been found. Urological opinion was that surgery would not help him. Repeated urinary infections had occurred, many different organisms having been cultured from his urine, despite every care. His recurrent urinary infections had even included two spells of *Pseudomonas pyocyanea*. Up to the time of the meeting it had been found possible to eradicate the urinary organisms by antibiotics, given either singly or in combination. The laboratory sensitivity tests had given a valuable guide in that. He needed an indwelling catheter for part of the time, but after a few days the catheter could be removed without undue retention, the patient preferring to dispense with it. Antibiotics used to treat his urinary infections had included sulphonamides, penicillin, "Terramycin", "Chloromycetin", "Aureomycin", "Hibitane", neomycin and streptomycin. Therapy had also been by mephenesin, half a gramme twice a day, and subsequently mephenesin carbamate, to reduce the spasticity. As the usual prognosis given for such cases was one to two years, Dr. Southcott concluded that the survival for nine years could perhaps be taken as a tribute to modern antibiotics.

Dr. C. C. Jungfer stated that he had attended the patient in private. Although the diagnosis at present was well established, initially there had been some difficulties. Initially, consultant opinion in private had favoured a cerebral vascular origin of the disease.

On The Periphery.

TROUSERS IS TROUSERS, BUT WHAT IS DOCTORS?

RECENTLY, at night, a Melbourne doctor attended a boy who had been bitten by a dog. At the first visit the youth's wounds were cleaned and dressed and tetanus toxoid was injected. He was examined again on the following day. The owner of the dog has accepted liability for expenses, and has paid £3 14s. for damage to the boy's trousers, but claims that the doctor's bill of £2 2s. 6d. is excessive.

Correspondence.

A REPRESENTATIVE BODY FOR THE B.M.A. IN AUSTRALIA.

SIR: Modern air transport has rendered practicable the functioning of a Representative Body for any Branch whose Council believes in representative government (e.g. one representative per electoral area). It is the Council (and not "the members") which can institute proceedings in the matter—just as the Cabinet did in the matter of a uniform divorce bill—if it has the wish or the will to do so.

Without prejudice, if the Council is unable to offer solutions to the problems of Dr. Klugman and Dr. McCluskie (MED. J. AUST., November 28, 1959), then perhaps the case for the inauguration of a Representative Body could be taken up through F.O.C.L.A. However, this would seem to be a difficult operation on a wide front for an understaffed headquarters with poor lines of communication. Veterans of old campaigns, and others equally entitled, may care to offer their appreciation of the situation.

Yours, etc.,

FRANCHISE.

Sydney,
December 2, 1959.

MEDICAL RESEARCH IN AUSTRALIA.

SIR: The letter of Sir Macfarlane Burnet is most opportune. It is necessary to take stock of the organization of medical research in Australia. This has been apparent to the Medical Research Advisory Committee of the National Health and Medical Research Council for some time.

In November, 1957, following on the issue of the Murray Report, a letter was forwarded to the Commonwealth Minister for Health by this Committee, requesting that the Prime Minister be asked to issue an invitation to Sir Harold Himsworth, Secretary of the Medical Research Council of Great Britain, to visit Australia and advise the Commonwealth Government on the organization and financial needs of medical research in Australia.

It is necessary, as Sir Macfarlane says, to take stock of the organization of medical research in Australia, and this could only be done by an impartial investigator from outside Australia.

The field of trained research workers capable of undertaking independent research work is strictly limited in Australia and, therefore, it is necessary for independent bodies making grants to have expert advice about projects and personnel. This advice could only come from a small body similar to the University Grants Commission, which had a permanent full-time secretary available at all times for advice.

Yours, etc.,

W. F. SIMMONS,
Chairman.

Medical Research Advisory Committee,
National Health and Medical Research Council,
Forest Road and Herbert Street,
Bexley, N.S.W.
January 25, 1960.

Post-Graduate Work.

ROYAL PRINCE ALFRED HOSPITAL: EAR, NOSE AND THROAT DEPARTMENT.

Seminar Programme, 1960.

THE staff of the ear, nose and throat department of the Royal Prince Alfred Hospital will conduct a seminar on the second Saturday of every month at 8 a.m. in the Scot Skirving Lecture Theatre. The main speaker will not exceed forty minutes, and there will be a discussion at the conclusion of his remarks. All medical practitioners and clinical students are invited to attend.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JANUARY 2 1960.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.[2]	Western Australia.	Tasmania.[2]	Northern Territory.	Australian Capital Territory.[2]	Australia.[2]
Acute Rheumatism	2(2)	2(1)	..	..	..	..	..	..	4
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	7	..	7
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	1	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	4(2)	2(2)	2	..	..	..	2	..	10
Diphtheria	..	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	..	2(2)	..	..	3(3)	..	..	..	5
Encephalitis	2	3(3)	..	..	..	..	..	..	5
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	22(9)	15(9)	11	..	5(2)	..	1	..	54
Lead Poisoning	..	..	1(1)	..	..	..	..	..	1
Leprosy	..	1(1)	..	..	..	..	1	..	2
Leptospirosis	..	..	3(1)	..	..	..	..	..	3
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	..	..	..	..	1	..	..	..	1
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1(1)	..	..	..	..	..	..	..	1
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	5(5)	..	..	1(1)	..	..	..	6
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	..	5(5)	4(1)	..	1(1)	..	..	..	10
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	2	..	2
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	10(7)	20(10)	12(4)	..	6(2)	..	..	..	48
Typhoid Fever	..	..	..	..	1(1)	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

[2] No return received from South Australia and Tasmania; nil return from Australian Capital Territory.

At the next seminar, to be held on February 13, 1960, Dr. H. D. Raffan will speak on "Papillomata of the Larynx".

Notes and News.

A Complimentary Dinner to Dr. Cecil Walters.

A complimentary dinner will be tendered to Dr. Cecil Walters at the University Club, Sydney, on Saturday, February 20, 1960, at 7 p.m. for 7.30 p.m. Those wishing to be present, especially old Coast Hospital resident medical officers, are asked to communicate with Dr. Eric Goulston, 135 Macquarie Street, Sydney, before February 11.

Corrigendum.

SEASONAL CONCEPTION RATES IN AUSTRALIA.

IN the paper entitled "Seasonal Conception Rates in Australia", by W. V. Macfarlane and D. Spalding, published *in our issue of January 23, 1960, on page 124, under* "Acknowledgements", Mr. E. C. Solomons, Statistician for Queensland, is wrongly described as Mr. D. Solomons.

Nominations and Elections.

THE undermentioned have applied for election as members *of the New South Wales Branch of the British Medical* Association:

Polner, Rudolph Rezso, M.D., 1949 (Univ. Budapest), (Regional Registration, Section 21A, Barellan Region), Box 62, Barellan.

Carmody, John Spohn, M.B., B.S., 1958 (Univ. Sydney), 3 Fisher Avenue, Vaucluse.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association (provisional registration being M.B., B.S., 1960 *(Univ. Sydney)): Armstrong, Michael Lawrence; Carney,* Donald Earl; Casey, Brian Hal; Frankland, Howard Edward; Miles, Neil MacKay; North, Robert Alan; Penny, *Ronald; Stevens, Susan Margaret Borradaile; Oldfield,* Allen Stanley; Swynny, Colleen Lessley; Warden, John Charles; Wells, John Vivian. Burgess, John Austin, M.B., *B.S., 1959 (Univ. Sydney); Munster, Andrew Michael, M.B.,* B.S., 1959 (Univ. Sydney); Francis, John Fulton, M.B., B.S., 1958 (Univ. Sydney); Seaton, Douglas George, M.B., B.S., *1954 (Univ. Sydney); Burkitt, Barbara Frances Emra,* M.B., B.S., 1958 (Univ. Sydney); Coupland, Graham Arthur Edwin, M.B., B.S., 1959 (Univ. Sydney); Gong, Lawrence *William, M.B., B.S., 1959 (Univ. Sydney); Hart, Graham* Hugh Basil, M.B., B.S., 1956 (Univ. Sydney); Jeremy, Ross, M.B., B.S., 1957 (Univ. Sydney); Knott, Bernays *Melville, M.B., B.S., 1958 (Univ. Sydney); Pritchard,* Elizabeth, M.B., B.S., 1958 (Univ. Sydney); Sinclair, Agnes Esther, M.B., B.S., 1958 (Univ. Sydney); Nedeljkovic, *Miroslav, Licence Section 21c (4), M.D., 1934 (Univ.* Belgrade).

Medical Appointments.

Dr. A. S. Ellis has been appointed as Psychiatrist, Mental Hygiene Branch, Department of Health, Victoria.

Dr. I. P. James has been appointed as Deputy Superintendent, Receiving House, Royal Park, Victoria.

Dr. D. O. Tonkin has been appointed as Honorary *Ophthalmologist, Parkside Mental Hospital, South Australia.*

Dr. R. A. Atherton has been appointed as Medical Superintendent, Mental Hospital, Ipswich, Queensland.

Deaths.

THE undermentioned deaths have been announced:

BALTRUNAS.—Stanley Baltrunas, on December 9, 1959, at Melbourne.

MILLER.—Robert Christie Miller, on January 24, 1960, at Sutherland.

INGLIS.—William Keith Inglis, on January 26, 1960, at Sydney.

Diary for the Month.

FEBRUARY 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
FEBRUARY 11.—New South Wales Branch, B.M.A.: Public Relations Committee.
FEBRUARY 12.—Queensland Branch, B.M.A.: Council Meeting.
FEBRUARY 12.—Tasmanian Branch, B.M.A.: Branch Council.
FEBRUARY 15.—Victorian Branch, B.M.A.: Finance Sub-committee.
FEBRUARY 16.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, *135 Macquarie* Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, *80 Brougham* Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should *be typed with double or treble spacing. Carbon copies should* not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, *and not to underline either words or phrases.*

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant *appointment and/or the unit, hospital or department from* which the paper comes.

References to articles and books should be carefully checked. *In a reference to an article in a journal the following* information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the *following information should be given: surname of author,* initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). *The abbreviations used for the titles of journals are those* of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, *together with that of the journal in which the abstract has* appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to *provide the originals (not photographic copies) of line* drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not *accustomed to preparing drawings or photographic prints for* reproduction are invited to seek the advice of the Editor.

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